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Green and black tea for the primary prevention of cardiovascular disease (Review)

Hartley L, Flowers N, Holmes J, Clarke A, Stranges S, Hooper L, Rees K

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[Intervention Review]

Green and black tea for the primary prevention of cardiovascular disease

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ABSTRACT

Background

There is increasing evidence that both green and black tea are beneficial for cardiovascular disease (CVD) prevention.

Objectives

To determine the effects of green and black tea on the primary prevention of CVD.

Search methods

We searched the following databases on 12 October 2012 without language restrictions: CENTRAL in *The Cochrane Library*, MEDLINE (OVID), EMBASE (OVID) and Web of Science (Thomson Reuters). We also searched trial registers, screened reference lists and contacted authors for additional information where necessary.

Selection criteria

Randomised controlled trials (RCTs) lasting at least three months involving healthy adults or those at high risk of CVD. Trials investigated the intake of green tea, black tea or tea extracts. The comparison group was no intervention, placebo or minimal intervention. The outcomes of interest were CVD clinical events and major CVD risk factors. Any trials involving multifactorial lifestyle interventions or focusing on weight loss were excluded to avoid confounding.

Data collection and analysis

Two review authors independently selected trials for inclusion, abstracted data and assessed the risk of bias. Trials of green tea were analysed separately from trials of black tea.

Main results

We identified 11 RCTs with a total of 821 participants, two trials awaiting classification and one ongoing trial. Seven trials examined a green tea intervention and four examined a black tea intervention. Dosage and form of both green and black tea differed between trials. The ongoing trial is examining the effects of green tea powder capsules.

No studies reported cardiovascular events.

Black tea was found to produce statistically significant reductions in low-density lipoprotein (LDL) cholesterol (mean difference (MD) -0.43 mmol/L, 95% confidence interval (CI) -0.56 to -0.31) and blood pressure (systolic blood pressure (SBP): MD -1.85 mmHg, 95% CI -3.21 to -0.48. Diastolic blood pressure (DBP): MD -1.27 mmHg, 95% CI -3.06 to 0.53) over six months, stable to sensitivity analysis, but only a small number of trials contributed to each analysis and studies were at risk of bias.

Green tea was also found to produce statistically significant reductions in total cholesterol (MD -0.62 mmol/L, 95% CI -0.77 to -0.46), LDL cholesterol (MD -0.64 mmol/L, 95% CI -0.77 to -0.52) and blood pressure (SBP: MD -3.18 mmHg, 95% CI -5.25 to -1.11; DBP: MD -3.42, 95% CI -4.54 to -2.30), but only a small number of studies contributed to each analysis, and results were not stable to sensitivity analysis. When both tea types were analysed together they showed favourable effects on LDL cholesterol (MD -0.48 mmol/L, 95% CI -0.61 to -0.35) and blood pressure (SBP: MD -2.25 mmHg, 95% CI -3.39 to -1.11; DBP: MD -2.81 mmHg, 95% CI -3.77 to -1.86). Adverse events were measured in five trials and included a diagnosis of prostate cancer, hospitalisation for influenza, appendicitis and retinal detachment but these are unlikely to be directly attributable to the intervention.

Authors' conclusions

There are very few long-term studies to date examining green or black tea for the primary prevention of CVD. The limited evidence suggests that tea has favourable effects on CVD risk factors, but due to the small number of trials contributing to each analysis the results should be treated with some caution and further high quality trials with longer-term follow-up are needed to confirm this.

PLAIN LANGUAGE SUMMARY

Green and black tea to prevent cardiovascular disease

Cardiovascular disease (CVD) is a worldwide healthcare burden. However, it is thought that CVD risk can be lowered by changing a number of modifiable risk factors such as diet, and this includes the intake of tea. This review assessed the effectiveness of green tea, black tea or black/green tea extracts in healthy adults and those at high risk of CVD. We found 11 randomised controlled trials, four of which examined black tea interventions and seven examined green tea interventions. There were variations in the dosage and form (drink, tablets or capsules) of the black and green tea interventions, and the duration of the interventions ranged from three months to six months. Adverse events were reported in five of the included trials. These included a diagnosis of prostate cancer, hospitalisation for influenza, appendicitis and retinal detachment; these are unlikely to be associated with the intervention. The results showed black and green tea to have a beneficial effect on lipid levels and blood pressure, but these results were based on only a small number of trials that were at risk of bias. Analysis conducted over both tea types showed beneficial effects of tea on LDL-cholesterol and blood pressure but again this was based on only a few trials that were at risk of bias. To date the small number of studies included suggest some benefits of green and black tea on blood pressure and lipid levels but more longer-term trials at low risk of bias are needed to confirm this.

BACKGROUND

Description of the condition

Cardiovascular diseases (CVD) are the result of complications in the heart and blood vessels (WHO 2011), and include cerebrovascular disease, coronary heart disease (CHD), and peripheral arterial disease (PAD). Around 29.6% of total global deaths can be attributed to CVD (World Health Report 2003) and it is estimated that 17 million deaths per year are caused by CVD (Mackay 2004).

One of the main mechanisms thought to cause CVD is atherosclerosis, where the arteries become blocked by plaques or atheromas (NHS 2010). Atherosclerosis can cause CVD when the arteries are completely blocked by a blood clot or when blood flow is restricted by a narrowed artery limiting the amount of blood and oxygen that can be delivered to organs or tissue (British Heart Foundation 2012). While arteries may naturally become harder and narrower with age this process may be accelerated by factors such as smoking, high cholesterol, high blood pressure, obesity, a sedentary lifestyle and ethnicity (NHS 2010). Ruptures of unstable plaque can also lead to CVD. Unstable plaques are thought to activate an inflammatory response in the body. This inflammatory response causes the structure of atherosclerotic plaque to weaken and rupture leading to the formation of blood clots (Spagnoli 2007).

A number of dietary factors have been found to be associated with CVD risk such as a low consumption of fruit and vegetables (Begg 2007), a high intake of saturated fat (Siri-Tarino 2010) and a high consumption of salt (He 2011). These factors are important since they can be modified in order to lower CVD risk making them a prime target for interventions aimed at primary prevention and management of CVD.

Description of the intervention

According to Deka (Deka 2011), records show tea has been used largely due to its medicinal purposes from as far back as the 10th century and it is now consumed worldwide. Tea leaves come from the plant *Camillia sinesis* and there are three main types of tea: green, black and oolong. The type of tea produced from the leaves depends on how the leaves are processed. For instance, partly fermented leaves produce oolong tea, fermented leaves produced black tea while non-fermented leaves create green tea (Deka 2011).

All types of tea made from *Camillia sinesis* are rich in flavonoids. These are water-soluble plant pigments that belong to the larger group of polyphenolic compounds (Corradini 2011; Scalbert 2005). The main class of flavonoids found in tea are flavanols. These include epigallocatechin (EGC), epigallocatechin gallate (EGCG), epicatechin gallate (ECG) and epicatechin (EC) (Kris-Etherton 2002). Whilst the total flavonoid content in green and black tea is similar, their chemical structures differ. This is mainly due to the oxidation process used in the manufacture of black tea that converts flavonoids, such as catechin found in green tea, into more complex varieties, mainly thearubigins and theaflavins (Deka 2011; Stangl 2006). In green tea catechin constitutes around 80% to 90% of total flavonoids, whereas in black tea they account for 20% to 30% of total flavonoids (Stangl 2006).

Green tea is also thought to have a high content of vitamins and minerals with five cups a day providing between 5% to 10% of a person's daily requirement of riboflavin, niacin, folic acid and pantothenic acid. Furthermore, this amount of green tea a day provides 45% of the daily requirement of manganese, 25% of potassium and 5% of magnesium (Shukla 2007).

How the intervention might work

Observational, epidemiological and experimental evidence have indicated that the consumption of green and black tea may have a beneficial effect on cardiovascular function (Deka 2011; Kuriyama 2008; Mineharu 2010; Nagao 2007; Sesso 1999). In particular, observational studies suggest that a high intake of both green and black tea is related to a reduction in CVD risk (Kuriyama 2008; Sesso 1999). For example, de Koning Gans et al (de Koning Gans 2010), in a prospective cohort study of 37,514 participants in the Netherlands, found that consuming three to six cups of tea (mainly black tea) a day was associated with a reduction in the risk of CHD mortality (hazard ratio (HR) = 0.55, 95% confidence interval (CI) 0.31 to 0.97) (cup size was not stated in the article). This is supported by Mineharu et al (Mineharu 2010) who reported a strong inverse relationship between the intake of more than six cups of green tea daily and CVD mortality in a cohort of 76,979 Japanese adults. These observational findings, however, must be cautiously interpreted because of the potential for confounding effects by factors commonly associated with tea drinking, such as healthier lifestyles, which might contribute to the observed inverse associations. Indeed, some studies have failed to show any relationship between the intake of tea and CVD risk (Brown 1993; Hertog 1997).

Meta-analyses of observational studies corroborate the findings from individual studies showing an inverse relationship between tea and CVD risk (Arab 2009; Peters 2001). Peters and colleagues examined the association between tea and CVD by analysing 10 cohort studies and seven case-control studies (Peters 2001). They found an 11% reduction in the risk of myocardial infarction when consuming three or more cups of tea a day. However, these authors suggest that their findings must be cautiously interpreted since there was evidence of publication bias of smaller positive studies.

Evidence from intervention studies also show the benefit of tea consumption in reducing the risk factors for CVD (Brown 2009; Nagao 2007). Fujita et al. (Fujita 2008), for instance, conducted a randomised double-blind placebo-controlled study to investigate the benefits of taking black tea extract in 47 Japanese patients with borderline hypercholesterolaemia. They found that black tea extract significantly lowered patients low-density lipoprotein (LDL) cholesterol and blood total cholesterol levels. A systematic review that searched for RCTs until 2006 and included 12 trials of green tea, and 12 of black tea compared with control (all assessed as at moderate to high risk of bias) found little effect of either type of tea on systolic or diastolic blood pressure or high-density lipoprotein (HDL) cholesterol (Hooper 2008). However, it was not stated in the primary studies of this review whether tea was caffeinated or decaffeinated. This is important since the impact of tea on CVD risk factors may be due, in part, to the acute effects of caffeine. Nonetheless, there was some evidence from moderate to poor quality trials that green tea reduced LDL cholesterol (black tea had no effect) and black tea improved flow mediated dilatation, an emerging risk factor for CVD (Hooper 2008). None of the included studies assessed mortality or cardiovascular events.

A more recent systematic review examined green tea consumption and its antioxidant effects in 31 controlled intervention studies published up to June 2010 (Ellinger 2011). The findings indicated

that there was some evidence that regular green tea consumption of at least 0.6 - 1.5 L/day reduced lipid peroxidation and increased antioxidant capacity. Ellinger et al (Ellinger 2011) therefore concluded that there was evidence, although limited, for the antioxidant effects of green tea which are suggested to protect against CVDs. However, many of the included studies were very short term and it is unclear whether benefits are sustained over longer periods.

The reduction of CVD risk by tea may be largely due to the high levels of polyphenols, in particular flavonoids, which both green and black tea contain. However, the exact mechanisms through which increased tea consumption reduces CVD risk are unknown. Some potential mechanisms include reducing weight, improving insulin sensitivity, improving dyslipidaemia, improving endothelial function by lowering oxidative stress, platelet inhibition and anti-inflammatory effects (Deka 2011). Furthermore, tea and their flavonoids have antioxidant properties that help to reduce CVD risk (Deka 2011; Gardner 2007).

Why it is important to do this review

Tea is the second most consumed beverage worldwide after water (Kris-Etherton 2002) and due to such high frequency of intake worldwide, even a small impact of tea on human health could have large implications for public health (Peters 2001). However, there is still inconclusive evidence from interventional and observational studies of tea consumption on clinical cardiovascular endpoints. An up-to-date systematic review is needed to clarify the association between tea consumption and CVD risk, which will then provide guidance for national and international governments, local authorities, practitioners and members of the public.

The current review updates and expands the most recent systematic reviews (Ellinger 2011; Hooper 2008). We have included only randomised controlled trials of either green or black tea and examined the effects over longer time periods (at least three months) as these are most relevant for public health interventions.

OBJECTIVES

The primary objective was to determine the effectiveness of green and black tea consumption for the primary prevention of CVD.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs). Cross-over trials were eligible for inclusion in this review if identified, but we would have used data only from the first half as a parallel group design.

Types of participants

Adults aged 18 and over from the general population and adults at high risk of CVD. This review focused on the effects of green and black tea intake on participants in primary prevention trials. We therefore excluded studies where more than 25% of participants had CVD at baseline including those who have experienced a previous myocardial infarction (MI), stroke, revascularisation procedure (coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA)), those with angina, or angiographically-defined CHD, cerebrovascular disease (stroke) and PAD. We also excluded studies where more than 25% of the participants had type 2 diabetes. While patients with type 2 diabetes are at increased risk of CVD, interventions for diabetes are covered specifically by the Cochrane Metabolic and Endocrine Disorders review group.

Types of interventions

The intervention was the intake of green or black tea as a beverage or the intake of tea extracts. No limit was placed on the amount of tea consumed. Studies examining green tea and green tea extracts were examined separately from those examining black tea and black tea extracts. We intended to examine the effect of "dose" and duration of tea intake if there were sufficient studies, and the effects of caffeine intake.

We focused on follow-up periods of six months or more as these are most relevant for public health interventions, and considered trials with follow-up periods of three months or more where longer term trials were lacking. Trials were only considered where the comparison group was no intervention, placebo or minimal intervention (e.g. leaflet to follow a dietary pattern with no person-to-person intervention or reinforcement). Trials using multifactorial lifestyle interventions and trials focusing on weight loss were excluded from the review to avoid confounding.

Types of outcome measures

Primary outcomes

1. Cardiovascular mortality
2. All-cause mortality
3. Non-fatal endpoints such as MI, CABG, PTCA, angina, or angiographically-defined CHD, stroke, carotid endarterectomy, or PAD

Secondary outcomes

1. Changes in blood pressure (systolic and diastolic blood pressure) and blood lipids (total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides)
2. Occurrence of type 2 diabetes as a major CVD risk factor
3. Health-related quality of life
4. Adverse effects
5. Costs

Search methods for identification of studies

Electronic searches

We searched the following electronic databases without language restrictions on 12 October 2012:

- Cochrane Central Register of Controlled Trials (CENTRAL) (Issue 9 of 12, September 2012) in *The Cochrane Library*;
- MEDLINE (OVID) (1946 to Week 1 October 2012);
- EMBASE Classic + EMBASE (OVID) (1947 to 2012 Week 40);
- Web of Science (Thomson Reuters) (1970 to 12 October 2012);
- Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment Database (HTA) and Health Economics Evaluations Database (HEED) (Issue 3 of 4, July 2012) on *The Cochrane Library*.

Medical subject headings (MeSH) or equivalent and text word terms were used. The Cochrane sensitive-maximising RCT filter (Lefebvre 2011) was used for MEDLINE and adaptations of it were used for EMBASE and Web of Science.

Searches were tailored to individual databases. The search strategies are shown in Appendix 1.

Searching other resources

We checked reference lists of reviews and retrieved articles for additional studies.

We searched the metaRegister of controlled trials (mRCT) (www.controlled-trials.com/mrct), Clinical trials.gov (www.clinicaltrials.gov), the WHO International Clinical Trials Registry platform (ICTRP) (http://apps.who.int/trialsearch/) for ongoing trials and Google Scholar for additional studies. We also searched OpenGrey to identify any relevant grey literature.The search strategies are shown in Appendix 2.

We also performed citation searches on key articles. We contacted experts in the field for unpublished and ongoing trials and authors were contacted where necessary for any additional information.

Data collection and analysis

Selection of studies

Two review authors (Louise Hartley (LH), Nadine Flowers (NF)) reviewed the title and abstract of each paper and retrieved potentially relevant references. We then obtained the full text of potentially relevant studies and the same two authors (LH, NF) independently selected studies to be included in the review by using predetermined inclusion criteria. In all cases we resolved all disagreements about study inclusion by consensus and consulted a third review author (Karen Rees (KR)) if disagreements persisted.

Data extraction and management

Two review authors independently (LH, NF or Jennifer Holmes (JH)) extracted data using a proforma. We also contacted chief investigators to provide additional relevant information when necessary. Details of the study design, participant characteristics, study setting, intervention (including number of components, tea or extract, duration, flavonoid and caffeine dose), and outcome data (including details of outcome assessment, adverse effects) and methodological quality (randomisation, blinding and attrition) were extracted from each included study. We resolved any disagreements about extracted data by consensus and consulted a third author (KR) if disagreements persisted.

Assessment of risk of bias in included studies

We assessed risk of bias by examining the random sequence generation and allocation concealment, description of drop-outs and withdrawals (including analysis by intention-to-treat), blinding (participants, personnel and outcome assessment) and selective outcome reporting (Higgins 2011) in each trial. Two authors (LH, NF) independently assessed the risk of bias of included studies and rated each domain as having a low risk of bias, a high risk of bias or an unclear risk of bias.

Measures of treatment effect

Data were processed in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). For continuous outcomes net changes were compared (i.e. intervention group minus control group differences) and a mean difference (MD) and 95% confidence interval (CIs) calculated for each study.

Assessment of heterogeneity

For each outcome, tests of heterogeneity were conducted (using the Chi^2 test of heterogeneity and I^2 statistic). Where there was no heterogeneity a fixed-effect meta-analysis was performed. If substantial heterogeneity (I^2 greater than 50%) was detected the review authors looked for possible explanations for this (for example, participants and intervention). If the heterogeneity could not be explained, the review authors considered the following options: provide a narrative overview and not aggregate the studies at all or use a random-effects model with appropriate cautious interpretation.

Subgroup analysis and investigation of heterogeneity

Results were stratified by i) black tea, ii) green tea. It was our intention to stratify studies by “dose” of tea intake and duration of the intervention but there were insufficient trials that met the inclusion criteria to do this. Similarly, the lack of included studies meant that we were unable to examine the effects of caffeine intake.

Sensitivity analysis

We carried out sensitivity analysis excluding studies with inadequate or unclear allocation concealment. There were insufficient trials to examine the effects of publication bias using funnel plots and tests of asymmetry (Egger 1997).

RESULTS

Description of studies

Results of the search

The searches generated 2319 hits and 1736 after de-duplication. Screening the titles and abstracts identified 135 papers for formal inclusion or exclusion. Of these, 11 RCTs (12 papers) met the inclusion criteria. We identified one ongoing trial (one paper) and there are two trials (two papers) awaiting classification. Details of the flow of studies through the review are given in Figure 1.

Figure 1. Study flow diagram.

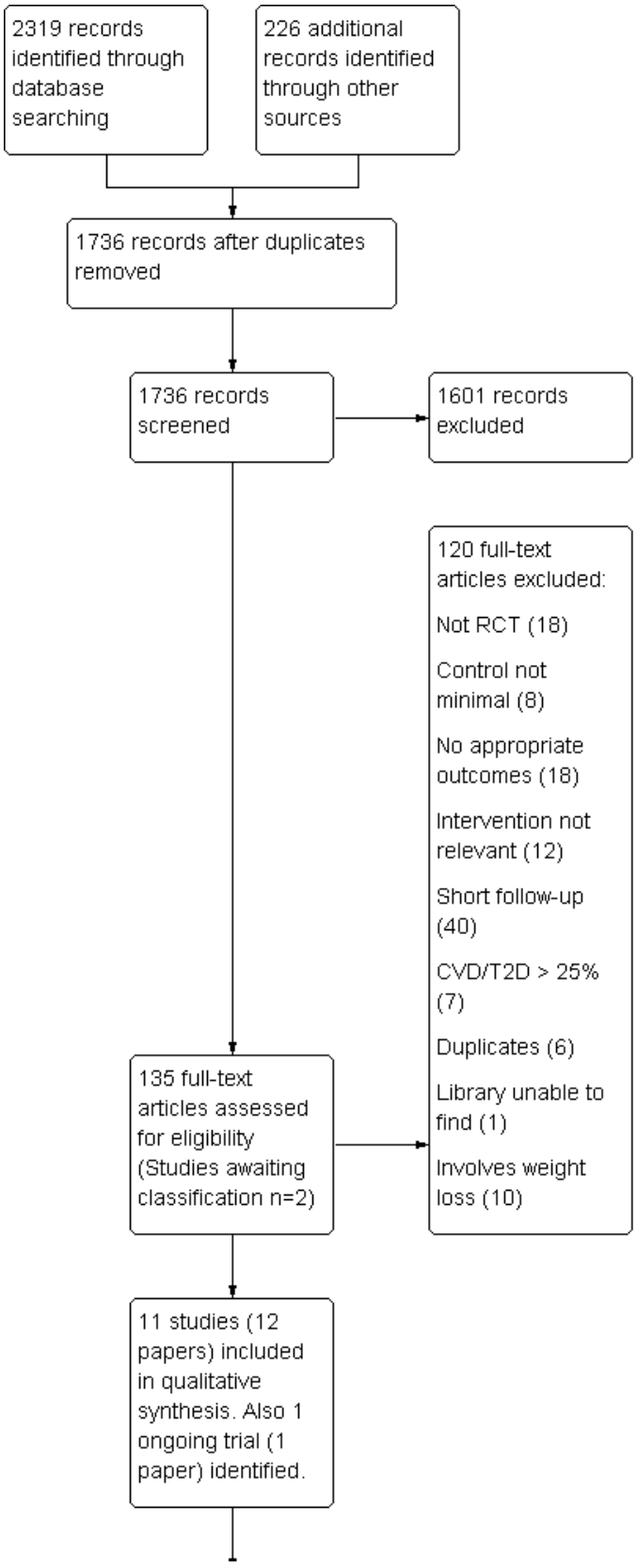
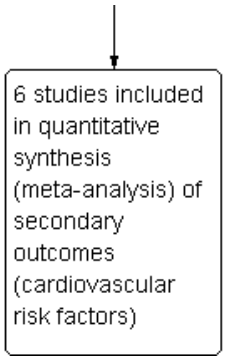


Figure 1. (Continued)



Included studies

Details of the methods, participants, intervention, comparison group and outcome measures for each of the studies included in the review are shown in the Characteristics of included studies table. Eleven trials with 11 trial arms were included with 821 participants randomised. None of the included studies reported on both black and green tea.

Four included studies examined black tea (Bahorun 2012; Fujita 2008; Hodgson 2012; Mukamal 2007). The health status of participants varied between studies; one of the studies recruited participants with borderline, or mild to moderate hypercholesterolaemia (Fujita 2008); one study recruited participants with either diabetes or two other cardiovascular disease risk factors (Mukamal 2007) and the remaining studies recruited healthy participants (Bahorun 2012; Hodgson 2012;). All four trials examining black tea recruited both male and female participants. One trial was conducted in the USA (Mukamal 2007) while the other studies were conducted in Japan (Fujita 2008), Mauritius (Bahorun 2012) and Australia (Hodgson 2012). The duration of the intervention and follow-up periods varied between three months (Bahorun 2012; Fujita 2008) and six months (Hodgson 2012; Mukamal 2007).

All four studies used black tea extracts, in tablet form (Fujita 2008) or as a drink (Bahorun 2012; Hodgson 2012; Mukamal 2007). Again, the dosage and type of black tea extracts varied between studies; 1 g black tea extract per day (Fujita 2008); 1.29 g black tea polyphenols per day (Hodgson 2012); three servings of 200 mL of black tea a day (Bahorun 2012) and 318 mg black tea catechins per day (Mukamal 2007).

Seven of the included studies examined green tea (Bogdanski 2012; Janjua 2009; Maron 2003; Nantz 2009; Shen 2010; Smith 2010; Stendell-Hollis 2010).

In these studies the health status of participants varied; one of the studies recruited participants with borderline, or mild to moderate hypercholesterolaemia (Maron 2003); one study recruited participants with hypertension (Bogdanski 2012); one study recruited breast cancer survivors (Stendell-Hollis 2010) and one recruited postmenopausal women with osteopenia (Shen 2010). The remaining three studies recruited healthy participants (Janjua 2009; Nantz 2009; Smith 2010). Four trials examining green tea recruited female participants only (154 randomised) (Janjua 2009; Shen 2010; Smith 2010; Stendell-Hollis 2010). Five trials were conducted in the USA (Janjua 2009; Nantz 2009; Shen 2010; Smith 2010; Stendell-Hollis 2010). The remaining studies were conducted in China (Maron 2003) and Poland (Bogdanski 2012). The duration of the intervention and follow-up periods varied between three months (Bogdanski 2012; Maron 2003; Nantz 2009; Smith 2010), six months (Shen 2010; Stendell-Hollis 2010) and two years (Janjua 2009).

Five of the studies used green tea extracts, in the form of tablets or capsules. Dosage and type of green tea extracts varied between studies; 500 mg per day of green tea polyphenols (Shen 2010); 375 mg green tea extract (Bogdanski 2012); 250 mg twice a day of green tea polyphenols (Janjua 2009); 200 mg theanine and 400 mg decaffeinated catechin green tea extract per day (Nantz 2009); and 75 mg theaflavins, 150 mg green tea catechins, and 150 mg other tea polyphenols per day (Maron 2003). One study provided participants with one beverage a day containing green tea extract (Smith 2010) while the remaining study provided participants with green tea bags containing 58.91 mg of catechins (Stendell-Hollis 2010).

One ongoing trial (one paper) was identified. Details of this trial are provided in the Characteristics of ongoing studies table. Briefly, the trial (Mitsuhiro Yamada 2009) examines the effects of 10 green tea powder capsules three times a day for 12 weeks in adults prone to metabolic syndrome. The outcomes measured include blood pressure and lipid levels. No anticipated end date was provided for this trial.

Excluded studies

Details and reasons for exclusion for the studies that most closely missed the inclusion criteria are presented in the Characteristics of excluded studies table. Reasons for exclusion for the majority of studies was their short-term duration (< three months). Other reasons for exclusion include the control not being a minimal intervention or no intervention/placebo, and no outcomes of interest.

Short-term studies

As stated above, the reason for exclusion for the majority of studies was that they were short term (< three months follow-up). We focused on three or more months follow-up as we were interested in the sustained effects of tea intake which are most relevant for public health interventions. Other systematic reviews have included some of these short-term studies (Ellinger 2011) and for interest we have listed them in Table 1.

Risk of bias in included studies

Details are provided for each of the included studies in the 'Risk of bias' tables in Characteristics of included studies and summarised in Figure 2; Figure 3.

Figure 2. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

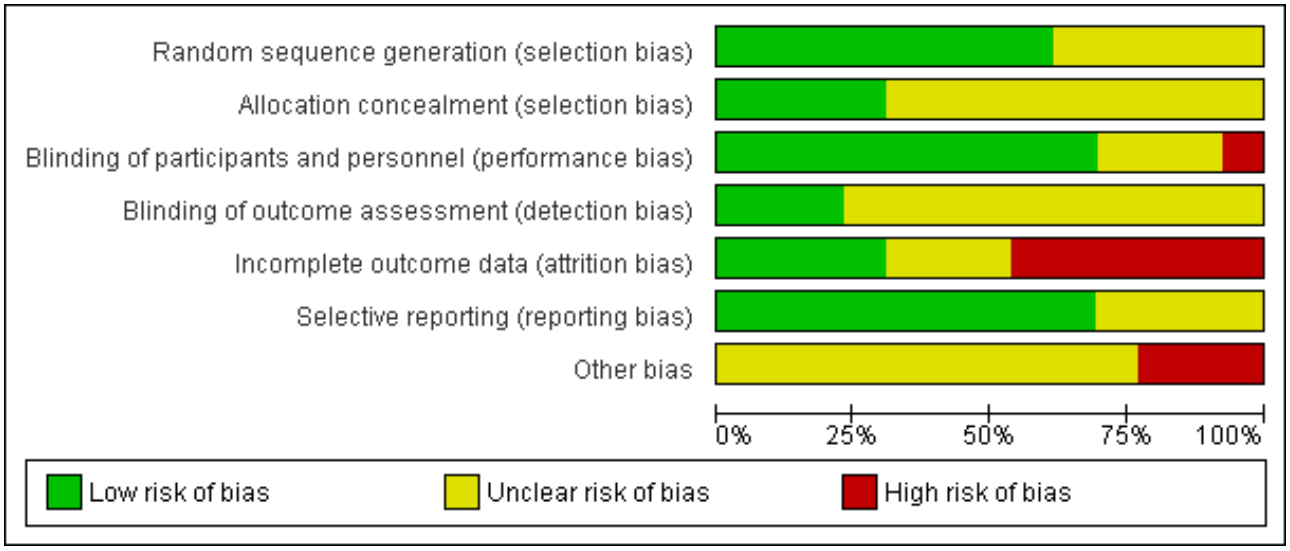
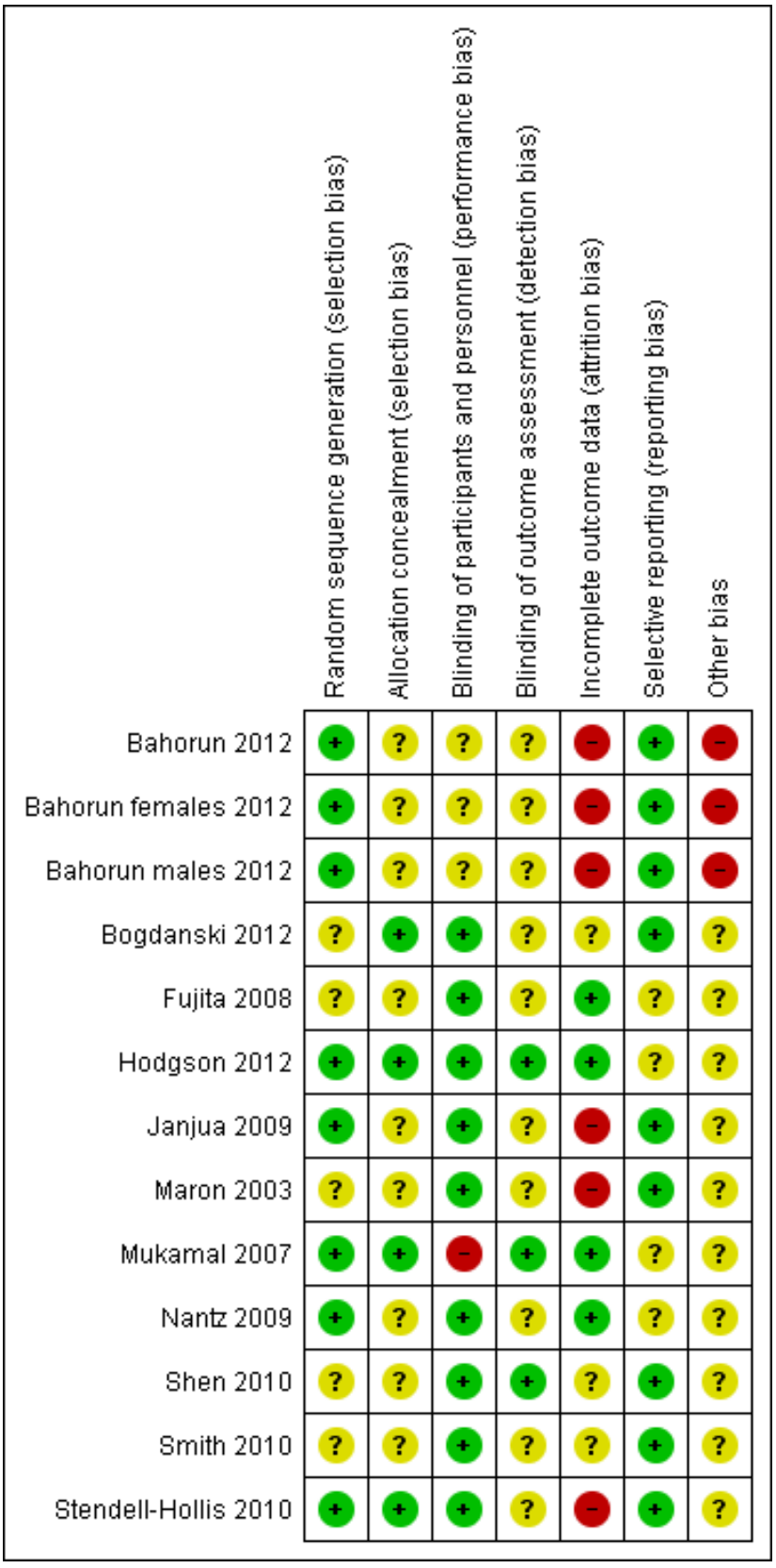


Figure 3. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Three of the trials that examined black tea clearly stated the methods of random sequence generation (Bahorun 2012; Hodgson 2012; Mukamal 2007) and were judged to be of low risk of bias. The methods of allocation concealment were not stated in two of the studies that examined black tea. In the two trials where this was clear, the methods were judges to be of low risk of bias (Hodgson 2012; Mukamal 2007).

The methods of random sequence generation were unclear in four of the green tea trials (Bogdanski 2012; Maron 2003; Shen 2010; Smith 2010). In the three trials where this was clear, the methods used were judged to be of low risk of bias (Janjua 2009; Nantz 2009; Stendell-Hollis 2010). Allocation concealment methods were not stated in five of the seven green tea trials. In the remaining two trials, the methods of allocation concealment were clear and so judged to be of low risk of bias (Bogdanski 2012; Stendell-Hollis 2010).

Blinding

Two trials examining black tea stated that they were double blind (participants and personnel were blind to treatment allocation, as were outcome assessors) and were regarded at low risk of bias (Fujita 2008; Hodgson 2012). One trial was stated as single blind (participants were not blinded to treatment allocation, but outcome assessors were blinded to the treatment allocation) (Mukamal 2007) while one trial did not state if it had used blinding (Bahorun 2012).

All of the trials examining green tea stated that they were double blind and placebo-controlled and so were regarded as being at low risk of performance bias. However, in six of the trials no details were provided as to whether outcome assessors were blinded (Bogdanski 2012; Janjua 2009; Maron 2003; Nantz 2009; Smith 2010; Stendell-Hollis 2010) and so were regarded as being at unclear risk of detection bias.

Incomplete outcome data

Loss to follow-up was reported in all four of the black tea trials. Three of the four included studies were judged as low risk of bias as they clearly reported reasons for withdrawals, exclusions and losses to follow-up (Fujita 2008; Hodgson 2012; Mukamal 2007). Two of these studies had also performed intention-to-treat (ITT) analyses (Hodgson 2012; Mukamal 2007). One of the trials examining black tea was judged at high risk of bias as losses to follow-up had not been reported by group and no ITT analysis had been performed (Bahorun 2012).

Four of the seven trials looking at green tea reported loss to follow-up (Nantz 2009; Janjua 2009; Shen 2010; Stendell-Hollis 2010) and one trial was judged as low risk of bias as withdrawals and exclusions were clearly reported (Nantz 2009). Three studies were judged at high risk of bias as either losses to follow-up were not reported and no ITT analysis had been performed (Maron 2003), or losses to follow-up were unbalanced between groups and no ITT analysis was performed (Janjua 2009; Stendell-Hollis 2010). The remaining three studies were judged as unclear as in two studies no information on loss to follow-up was provided (Bogdanski 2012; Smith 2010) and in the third study no reasons were reported for loss to follow-up but an ITT analysis was performed (Shen 2010).

Selective reporting

Three of the four studies looking at black tea were judged as unclear as there was insufficient information to judge the risk of selective reporting (Fujita 2008; Hodgson 2012; Mukamal 2007). The remaining study was judged as low risk as all expected outcomes were reported (Bahorun 2012).

One study examining green tea was judged as unclear due to there being insufficient information to judge the risk of selective reporting (Nantz 2009). The remaining six trials have been judged as low risk as all expected outcomes were reported (Bogdanski 2012; Janjua 2009; Maron 2003; Shen 2010; Smith 2010; Stendell-Hollis 2010).

Other potential sources of bias

For studies of both black and green tea, there was insufficient information to judge the risk of bias from other potential sources.

Effects of interventions

Cardiovascular events

None of the included studies provided clinical event data.

Mortality

None of the included studies provided mortality data.

Cardiovascular risk factors

Black tea

Three of the four included trials examining the effects of black tea measured lipid levels (Bahorun 2012; Fujita 2008; Mukamal 2007) and contribute to the meta-analysis. For one study (Bahorun 2012), the reported results for all lipid measurements were split by gender.

For LDL-cholesterol (three studies, one study reporting males and females separately, 147 participants) moderate heterogeneity was observed between the studies (I^2 = 33%) so a random-effects meta-analysis was performed. From the pooled analysis, black tea was found to lower LDL-cholesterol (mean difference (MD) -0.43 mmol/L, 95% confidence interval (CI) -0.56 to -0.31) (Analysis 1.1). Results were similar for the fixed-effect model, the random-effects results were reported as the effect estimate is more conservative with wider confidence intervals. Sensitivity analysis, removing studies with unclear allocation concealment, retained one study and statistical significance (MD -0.39 mmol/L, 95% CI -0.54 to -0.24).

A random-effects meta-analysis was also conducted for HDL-cholesterol (three studies, one reporting males and females separately, 146 participants) where heterogeneity was again observed between studies (I^2 = 36%). We found no evidence of effect of black tea on HDL levels in the four trials reporting this (Analysis 1.2).

For triglyceride levels, significant heterogeneity existed between the trials (three studies, one reporting males and females separately, I^2 = 64%) and a meta-analysis was not performed (Analysis 1.3). In one trial, black tea was found to significantly reduce triglyceride levels (MD -0.17 mmol/L. 95% CI -0.30 to -0.04) (Fujita 2008) whilst for female participants in another trial, triglycerides were found to increase in those given black tea (MD 0.55 mmol/L, 95% CI -0.01 to 1.11) but this was not statistically

significant (Bahorun 2012). For their male counterparts, black tea was found to have no effect on triglyceride levels (MD -0.32 mmol/L, 95% CI -1.06 to 0.42) (Bahorun 2012), a finding supported by the final study (MD 0.03 mmol/L, 95% CI -0.17 to 0.23) (Mukamal 2007) (and the only study with low risk of bias from allocation concealment).

Two trials (one reporting males and females separately) of black tea measured total cholesterol levels (Bahorun 2012; Fujita 2008) (Analysis 1.4). However, significant heterogeneity was found to exist between the trials (I^2 = 84%) and therefore a meta-analysis was not performed. One trial showed a statistically significant reduction in total cholesterol (MD -0.54 mmol/L, 95% CI -0.63 to -0.45) (Fujita 2008) whilst in the second trial black tea was found to have no effect on total cholesterol in females (MD 0.41 mmol/L, 95% CI -0.19 to 1.01) or males (MD 0.00 mmol/L, 95% CI -0.59 to 0.59) (Bahorun 2012).

Two included trials examined the effect of black tea on blood pressure (Hodgson 2012; Mukamal 2007). The meta-analysis (123 participants) showed a statistically significant reduction in systolic blood pressure (SBP) (MD -1.85 mmHg, 95% CI -3.21 to -0.48) (Analysis 1.5). Diastolic blood pressure (DBP) (123 participants) was also reduced with the black tea intervention, however, this result did not reach statistical significance (MD -1.27 mmHg, 95% CI -3.06 to 0.53) (Analysis 1.6). Sensitivity analysis removing studies at unclear risk of bias from allocation concealment did not remove either study, so results were unchanged.

Green tea

Four of the seven included trials examined the effects of green tea on lipid levels (Bogdanski 2012; Maron 2003; Smith 2010; Stendell-Hollis 2010) and so contributed to the meta-analysis. From the pooled analysis, the green tea intervention showed a statistically significant reduction in total cholesterol (327 participants) (MD -0.62 mmol/L, 95% CI -0.77 to -0.46) (Analysis 2.1) and LDL-cholesterol (327 participants) (MD -0.64 mmol/L, 95% CI -0.77 to -0.52) (Analysis 2.2) compared to placebo. For triglycerides (327 participants) the pooled analysis found green tea to lower triglyceride levels (MD -0.08 mmol/L, 95% CI -0.24 to 0.07) (Analysis 2.3), however, this result did not reach statistical significance.

For HDL cholesterol (four studies, 327 participants), moderate heterogeneity was found between studies (I^2= 39%) so a random-effects meta-analysis was performed (Analysis 2.4). From the pooled analysis, there was no evidence of effect of green tea on HDL cholesterol levels (MD 0.01 mmol/L, 95% CI -0.08 to 0.11). Results were similar for the fixed-effect model; the random-effects results were reported as the effect estimate is more conservative with wider confidence intervals. Sensitivity analysis, removing studies with unclear allocation concealment, retained one study (MD -0.10 mmol/L, 95% CI -0.27 to 0.07).

Three trials examining green tea measured blood pressure (Bogdanski 2012; Nantz 2009; Smith 2010) but one did not provide any individual group data and could not be included in a meta-analysis. The pooled analysis showed a statistically significant reduction in SBP (167 participants) (MD -3.18 mmHg, 95% CI -5.25 to -1.11) (Analysis 2.5) and DBP (167 participants) (MD -3.42, 95% CI -4.54 to -2.30) (Analysis 2.6) in the green tea group. The trial not included in the meta-analysis showed no significant change in blood pressure in either the tea (SBP change 1.10%, DBP change -7.20%) or control group (SBP decrease 0%, DBP decrease 1.10%) (Smith 2010). For all three trials allocation concealment was unclear, and sensitivity analyses removed them from the pooled analysis.

All tea (Green and Black)

Six trials (four using green tea and two using black tea, one reporting males and females separately) measured total cholesterol levels (Bahorun 2012; Bogdanski 2012; Fujita 2008; Maron 2003; Smith 2010; Stendell-Hollis 2010). Significant heterogeneity (I^2 = 66%) was found between the trials and so a meta-analysis was not performed. Two of the four trials showed tea to significantly reduce total cholesterol (Fujita 2008; Maron 2003) while in two trials, tea was found to reduce total cholesterol but this result did not reach statistical significance (Bogdanski 2012; Smith 2010). In the remaining two trials, tea was found to have no effect on total cholesterol levels (Bahorun 2012; Stendell-Hollis 2010).

Seven trials (one examining males and females separately) looked at HDL-cholesterol (473 participants), LDL-cholesterol (474 participants) and triglyceride levels (476 participants) (three using black tea and four using green tea) and contributed to the meta-analysis (Bahorun 2012; Bogdanski 2012; Fujita 2008; Maron 2003; Mukamal 2007; Smith 2010; Stendell-Hollis 2010). For LDL cholesterol (I^2= 49%), HDL-cholesterol (I^2 = 33%) and triglycerides (I^2 = 37%), moderate heterogeneity was observed between the studies so random-effects meta-analyses were performed. The pooled analysis showed tea to significantly reduce LDL-cholesterol (MD -0.48 mmol/L, 95% CI -0.61 to -0.35) (Analysis 3.2), have no effect on HDL-cholesterol (MD 0.00 mmol/L, 95% CI -0.04 to 0.04) (Analysis 3.3) and decrease triglycerides (MD -0.06 mmol/L, 95% CI -0.19 to 0.06) (Analysis 3.4), although this did not reach statistical significance.

Five trials (three using green tea and two using black tea) measured blood pressure (Bogdanski 2012; Hodgson 2012; Mukamal 2007, Nantz 2009:Smith 2010). Only four of these contributed to the meta-analysis as one trial did not report individual group data (Smith 2010). The meta-analysis showed a statistically significant reduction in SBP (290 participants) (MD -2.25 mmHg, 95% CI -3.39 to -1.11) (Analysis 3.5) and DBP (290 participants) (MD -2.81 mmHg, 95% CI -3.77 to -1.86) (Analysis 3.6) with the tea intervention.

Adverse effects

Adverse effects were monitored in five trials. Generally, side effects were mild and not attributable to the tea interventions as there were no significant differences in adverse events between the treatment and placebo groups (Janjua 2009; Maron 2003; Nantz 2009; Shen 2010). However, in one study (Mukamal 2007), adverse events included a new diagnosis of prostate cancer and a single hospitalisation for influenza among participants assigned to tea and in another study adverse events in the tea group included appendicitis and retinal detachment (Janjua 2009).

Quality of Life

Quality of life was measured in one of the trials (Shen 2010). Supplementation of 500 mg green tea polyphenols (GTP) daily to postmenopausal osteopenic women for 24 weeks had no influence on quality of life (as assessed by SF-36 questionnaires).

Costs

None of the included studies provided data on costs.

DISCUSSION

Summary of main results

Eleven trials that randomised 821 participants in studies of three or more months duration were identified from the 1735 papers screened. Four of these examined black tea interventions and seven examined green tea interventions.

None of the trials measured clinical events or mortality as they were relatively short term and conducted in mainly healthy participants. The review showed that black tea produced a statistically significant reduction in LDL-cholesterol and systolic and diastolic blood pressure (stable to sensitivity analyses). For green tea statistically significant reductions were found in total cholesterol, LDL cholesterol and systolic and diastolic blood pressure but the studies contributing to these analyses were removed in sensitivity analyses. However, only a small number of trials contributed to these analyses, and most trials were very small. Only one trial looked at the effects of tea on health-related quality of life. Few adverse events were measured and none directly attributable to the intervention.

Overall completeness and applicability of evidence

This review included adult participants who were at varying levels of CVD risk and included both free-living men and women. Most of the trials were conducted in developed countries. None of the 11 included studies examined our primary outcomes as trials were relatively short term in follow-up and participants were predominantly healthy. We were also not able to examine the effects of "dose" or duration of the intervention, or the effects of caffeine intake due to the limited number of included trials. Furthermore, due to the varying doses of extracts/tea consumed between the included studies, we could not draw any conclusions about the number of cups of tea per day that would be required to reduce CVD risk factors.

The effectiveness of green tea could not be rigorously assessed as only four trials (447 participants) (Bogdanski 2012; Maron 2003; Nantz 2009; Smith 2010) examined cardiovascular risk factors at three months and one study at six months (39 participants) (Stendell-Hollis 2010). The remaining two trials examining green tea evaluated quality of life and adverse events over six months (Shen 2010) or adverse events over two years (Janjua 2009). Similarly, few trials were identified that examined the effectiveness of black tea. Four trials were found that measured cardiovascular risk factors (279 participants). Two of these had three months follow-up (Bahorun 2012; Fujita 2008) and two had six months follow-up (Hodgson 2012; Mukamal 2007).

One study examining black tea stratified lipid outcomes by gender (Bahorun 2012) and found differences in responses between men and women. Whilst there is well-established literature on differences in cardio-metabolic risk profiles between men and women (Mosca 2011), we cannot make any conclusions based on only one study. However, if sufficient evidence accrues, future updates of this review will examine the influence of gender on the outcomes of interest.

There was considerable variability in the interventions, participants recruited and outcomes measured in the included trials. The one ongoing trial will add to the evidence base but more trials are needed.

Quality of the evidence

The studies included in this review were at some risk of bias and as such, the results should be treated with caution. In five of the included trials the methods of random sequence generation were not stated or unclear while in seven trials the details of allocation concealment were not stated. Nine of the 11 included studies stated that they were double blind and in one trial, participants were not blinded to treatment allocation but outcome assessors were. Risk of bias related to incomplete outcome data was high in four studies, low in four studies and unclear in three studies. Bias due to selective outcome reporting was considered unclear in four studies and low in the remaining seven. For all studies there was insufficient information to judge the risk of other biases.

In addition, small study bias is a risk in this review as most trials were very small. We were unable to examine the effects of publication bias in funnel plots due to the limited number of included studies. However, small studies are often less methodologically robust, more likely to be conducted in selected populations and have been shown to report larger beneficial effects than larger trials (Nüesch 2010; Sterne 2000; Sterne 2001). The results of the review need to be interpreted with this in mind.

Potential biases in the review process

A comprehensive search was conducted across major databases for interventions involving black or green tea or tea extract. Systematic review reference lists were also screened and authors contacted when necessary. All screening, inclusion and exclusion and data abstraction were carried out independently by two review authors. Data entry and analysis were also conducted by two review authors.

Our decision to restrict this review to interventions only investigating black or green tea avoided the potential confounding effects of other behavioural interventions on our outcomes e.g. those involving exercise, different dietary interventions or interventions that focused on weight loss. However, this limited the number of trials eligible for inclusion. In addition, the small number of trials on which this review is based, limitations in reporting methodological quality, an unclear risk of bias in most trials and little or no data for primary or secondary outcomes mean that caution should be used when interpreting the results of this review.

Agreements and disagreements with other studies or reviews

To our knowledge, no other systematic review including only randomised controlled trials has been carried out solely to examine the effects of black and green tea in adults for the primary prevention of CVD. Other systematic reviews have looked at flavonoid consumption on cardiovascular risk, which include tea, but also other flavonoid-rich foods (Hooper 2008). As in our review, the review by Hooper et al (2008) (Hooper 2008) found no studies examining tea that assessed mortality or cardiovascular events.

Other systematic reviews have solely concentrated on the antioxidant effects of green tea consumption (Ellinger 2011) with findings providing some evidence that regular intake of green tea

(at least 0.6 to 1.5L/day) reduced lipid peroxidation and increased antioxidant capacity. However, we cannot directly compare the effects on CVD risk factors between the two reviews as Ellinger et al (2011) did not examine CVD risk factors and included very short-term studies which did not meet our inclusion criteria.

AUTHORS' CONCLUSIONS

Implications for practice

Few trials met the inclusion criteria for our review and none reported our primary outcomes. Small beneficial effects were seen in the four trials of black tea and in three trials of green tea on cardiovascular risk factors, which is promising. This is because small reductions in CVD risk factors, such as blood pressure and lipid levels, throughout a whole population may lead to large reductions in CVD incidence (Emberson 2004). However, studies included in this review were at some risk of bias and as such the results should be treated with caution. To confirm these findings high quality trials are needed that examine cardiovascular disease and its risk factors over a longer period of time. Furthermore, future trials may consider the use of teas rather than tea extracts due to their wider availability and lower cost. In doing this, however, future trials should also take into account the use of a placebo since in trials that use tea, the placebo is usually water and there may be beneficial affects related to an increase in water consumption. Given the limited evidence to date, this review does not make any recommendations about changing practice.

Implications for research

There is a lack of randomised controlled trials looking at the effects of black and green tea consumption for the primary prevention of CVD. In particular, there is a shortage of randomised controlled trials that examine the effects of black and green tea interventions over the long term and which would help to examine the effects of such interventions on CVD events. We also found no trials reporting economic evaluations of interventions involving black or green tea and found only one trial that reported health-related quality of life outcomes.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Bahorun 2012

Methods	RCT of parallel group design
Participants	87 healthy adults of either sex, aged 25-60 years were enrolled. Inclusion criteria: non-smoker or former smokers who had stopped for less than 6 months. alcohol intake of less than 2 standard drinks/day, postmenopausal women not receiving hormone replacement therapy and ejection fraction greater than 40%. Country of publication was Mauritius.
Interventions	Participants were required to consume 3 x 200 mL of black tea a day for 12 weeks. Those in the control group consumed the equivalent volume of hot water for 12 weeks. Follow-up period was at the end of the intervention period of 12 weeks.
Outcomes	Triglycerides, total cholesterol, LDL-cholesterol, HDL-cholesterol.
Notes	This study was a post-hoc analysis of a subgroup of patients used in a previous study that recruited both patients with Ischaemic heart disease and healthy participants. As such, it has unequal randomisation to intervention and control groups and has a high potential for bias.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A random generator was used by a statistician and randomisation was in a 7:3 ratio. However, this is a post-hoc analysis of only the healthy participants and the methods of randomisation apply to all participants of the study which will include those with Ischaemic heart disease. Therefore, the number of healthy participants randomised to each group was unequal, with more participants randomised to the intervention group than to the control.
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated

Bahorun 2012 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	No ITT analysis. Reasons for attrition not reported sufficiently.
Selective reporting (reporting bias)	Low risk	All outcomes stated are reported
Other bias	High risk	Post-hoc analysis of a previous study that included patients with Ischaemic heart disease. Randomisation not equal between groups and no rationale for the randomisation ratio of 7:3 was given.

Bahorun females 2012

Methods	Please see information provided above
Participants	
Interventions	
Outcomes	
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A random generator was used by a statistician and randomisation was in a 7:3 ratio. However, this is a post-hoc analysis of only the healthy participants and the methods of randomisation apply to all participants of the study which will include those with Ischaemic heart disease. Therefore, the number of healthy participants randomised to each group was unequal, with more participants randomised to the intervention group than to the control.
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	No ITT analysis. Reasons for attrition not reported sufficiently.

Bahorun females 2012 *(Continued)*

Selective reporting (reporting bias)	Low risk	All outcomes stated are reported
Other bias	High risk	Post-hoc analysis of a previous study that included patients with Ischaemic heart disease. Randomisation not equal between groups and no rationale for the randomisation ratio of 7:3 was given.

Bahorun males 2012

Methods	Please see information provided above	
Participants		
Interventions		
Outcomes		
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	A random generator was used by a statistician and randomisation was in a 7:3 ratio. However, this is a post-hoc analysis of only the healthy participants and the methods of randomisation apply to all participants of the study which will include those with Ischaemic heart disease. Therefore, the number of healthy participants randomised to each group was unequal, with more participants randomised to the intervention group than to the control.
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	No ITT analysis. Reasons for attrition not reported sufficiently.
Selective reporting (reporting bias)	Low risk	All outcomes stated are reported
Other bias	High risk	Post-hoc analysis of a previous study that included patients with Ischaemic heart disease. Randomisation not equal between groups and no rationale for the randomisation ratio of 7:3 was given.

Bogdanski 2012

Methods	RCT of parallel group design
Participants	56 obese adults of either sex, aged 30-60 years with hypertension were enrolled. Exclusion criteria: those with secondary hypertension and/or secondary obesity, diabetes, history of coronary artery disease, stroke, congestive heart failure, malignancy, history of use of any dietary supplements within three months before the study, current need for modification of antihypertensive therapy, abnormal liver, kidney or thyroid gland function, clinically significant inflammatory process within respiratory, digestive or genitourinary tract, or in the oral cavity, pharynx, or paranasal sinuses, history of infection in the month before the study, nicotine or alcohol abuse and/or any other condition that would make participation not in the best interest of the subject or could prevent, limit or confound the efficacy assessment. Country of publication was Poland.
Interventions	Participants were required to consume 1 capsule of green tea extract or a placebo with a morning meal for 3 months. Each green tea capsule contained 379 mg of green tea extract. The placebo capsule contained pure microcrystalline cellulose. Follow-up period was at the end of the intervention period of 3 months.
Outcomes	Blood pressure, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Low risk	Used an independent statistician
Blinding of participants and personnel (performance bias) All outcomes	Low risk	States double-blind and placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	States double-blind but provides no details
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information provided
Selective reporting (reporting bias)	Low risk	All expected outcomes were reported
Other bias	Unclear risk	Insufficient information to judge

Fujita 2008

Methods	RCT of parallel group design
Participants	50 adults of either sex, aged 40-70 years with borderline hypercholesterolaemia were enrolled in the study. Exclusion criteria: those under treatment of serious cardiac, renal, or hepatic diseases; those with history of gastrectomy, enterectomy, other gastrointestinal surgery, or hypothyroidism; those

Fujita 2008 *(Continued)*

	with alcohol abuse, insulin-dependent diabetes or secondary causes of hyperglycaemia, pancreatitis, or serious hypertension. Country of publication was Japan.
Interventions	Participants were required to consume 2 black tea extract (BTE) tablets or placebo tablets, 3 times daily before meals for 3 months. Each BTE tablet (250 mg) contained 166.5 mg BTE (66.6%) and various bulking agents, including sugar alcohol (12.4%), cellulose (10%), polysaccharide (2%), lubricating and glossing agents (5%) and other excipients (4%). This meant that participants ingested a total of 1 g/day of BTE. The placebo tablets contained dextrin (66.6%) instead of BTE. Study was conducted between June 2006 and October 2006. Follow-up period was at the end of the intervention period of 3 months.
Outcomes	Total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides
Notes	BTE tablets were circular and placebo tablets were square. Adverse effects were monitored, however, none were reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	States double-blind and placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	States double-blind but provides no details
Incomplete outcome data (attrition bias) All outcomes	Low risk	Reasons for exclusions provided
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge
Other bias	Unclear risk	Insufficient information to judge

Hodgson 2012

Methods	RCT of parallel group design
Participants	111 healthy men and women, aged 35 to 75 years were recruited from the general population and randomised to two arms - black tea (56 participants) and placebo (55 participants). Inclusion criteria: taking up to three antihypertensive medications. Any change in regular medication with the potential to influence vascular health resulted in withdrawal of the participant from the study. Baseline status within the black tea group, based on 46 participants: mean age 56.9; 33% male, 20% taking antihypertensive medication. Baseline status within the placebo group, based on 49 participants: mean age 56.3, 37% male, 29% taking antihypertensive medication. Country of publication was Australia.

Hodgson 2012 *(Continued)*

Interventions	Participants consumed 3 cups/day of 1493 mg powdered black tea solids containing 429 mg of polyphenols and 96 mg of caffeine for 6 months, or placebo, 3 cups/day which was matched in flavour and caffeine content, containing no tea solids. Follow-up period was at the end of the intervention period of 6 months.
Outcomes	Blood Pressure (systolic and diastolic)
Notes	Participants were regular tea drinkers

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Used computer-generated random numbers.
Allocation concealment (selection bias)	Low risk	Randomisation codes sealed in envelopes, produced independent of study researchers. Envelopes opened in consecutive order as participants entered into the study.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	States placebo-controlled and double-blind.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Analysis performed by biostatistician blinded to treatment allocation.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Used ITT analysis.
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge
Other bias	Unclear risk	Insufficient information to judge

Janjua 2009

Methods	RCT of parallel group design
Participants	56 healthy women aged 25-75 years were randomised to two arms -green tea extract (29 participants) and placebo (27 participants). Inclusion criteria:Facial Glogau Photoaging scale II or III and Fitzpatrick skin type I to III. Exclusion criteria: Used systemic retinoids within 6 weeks before the start of the study, had active facial dermatological conditions that might interfere with photo-aging assessments, history of cosmetic procedure to the face such as laser treatment, chemical peel and facelifts. Country of publication was the U.S.A.
Interventions	Participants were required to consume 1 capsule twice daily containing green tea extract or placebo for two years. Each active study capsule contained 250 mg of polyphenols (70%) of which were catechins. The capsules were 99.5% caffeine-free. The placebo capsule were identical in appearance to the active capsule. Follow-up period was at the end of the intervention period of 2 years.

Janjua 2009 *(Continued)*

Outcomes	Adverse events
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind and placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Double-blind but provides no details
Incomplete outcome data (attrition bias) All outcomes	High risk	No ITT analysis and 37.9 % of tea group and 37% of placebo group dropped out of study
Selective reporting (reporting bias)	Low risk	All expected outcomes reported
Other bias	Unclear risk	Insufficient information to judge

Maron 2003

Methods	RCT of parallel group design
Participants	240 adults (100 males, 140 females) with mild to moderate hypercholesterolaemia and on a low-fat diet were recruited from outpatient clinics in 6 urban hospitals in China. Participants were randomised to 2 arms - tea extract (120 participants, 44.2% male, mean age 54.4) and placebo (120 participants, 39.2% male, mean age 55.0). Exclusion criteria: a baseline triglyceride level of 350 mg/dL or greater (4.0 mmol/L), having uncontrolled hypertension (160/95 mmHg), active pulmonary, hematologic, hepatic, gastrointestinal or renal disease, premalignant or malignant disease, diabetes, thyroid dysfunction, a history of coronary heart disease or other atherosclerotic disease, or any pathological values among routine clinical chemistry or hematological parameters having consumed greater than 32% of daily energy from fat or had a body mass index of 35 or higher, taking any lipid-lowering medications or drugs that might interfere with lipid metabolism, taking cardiac or other vasoactive medications including antihypertensive drugs, thyroid hormones, oral contraceptives, cyclic hormone replacement therapy, dietary supplements (e.g., fish oils, niacin at doses 400 mg/d, or dietary fibre supplements), or antioxidants, and they were prohibited from taking these medications during the course of the study. Country of publication was China.
Interventions	Participants were required to consume 1 capsule containing a theaflavin-enriched green tea extract or placebo, each morning, for 12 weeks (June 7th 2001 to October 18th 2001). Each active study capsule contained 75 mg of theaflavins, 150 mg of green tea catechins, and 150 mg of other tea polyphenols.The placebo capsules were made from inert ingredients and were identical to the theaflavin-enriched

Maron 2003 *(Continued)*

	green tea extract capsules in weight, appearance, and odour. Follow-up period was at the end of the intervention period of 12 weeks.
Outcomes	Total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, adverse effects.
Notes	Authors were contacted for extra information on lipid levels. Authors responded.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated, only states stratified by hospital
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind and placebo-controlled
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Double-blind but provides no details
Incomplete outcome data (attrition bias) All outcomes	High risk	No ITT analysis. Reasons for attrition not reported sufficiently. 95% and 88% of participants completed the study in intervention and control groups respectively
Selective reporting (reporting bias)	Low risk	All expected outcomes were reported
Other bias	Unclear risk	Insufficient information to judge

Mukamal 2007

Methods	RCT of parallel group design
Participants	31 community-dwelling adults aged 55 years and older with either diabetes (21% in tea group and 7% in control group) or 2 other cardiovascular risk factors (hypertension, current smoking, LDL cholesterol >=130 mg/dL, high-density lipoprotein cholesterol > 40 mg/dL, or family history of premature coronary heart disease) were randomised to 2 arms - black tea extract (16 participants, mean age 66.6 years, 79% on statins at baseline) and control (15 participants, mean age 64.9 years, 57% on statins at baseline). Exclusion criteria: established cardiovascular disease (congestive heart failure; myocardial infarction; coronary, carotid, or peripheral arterial revascularisation procedure; stroke; angina; or intermittent claudication), contraindications to MRI (severe claustrophobia, intolerance to previous MRI examinations, pacemaker, intraauricular implants, or intracranial clips), atrial fibrillation (due to requirement for gated MRI images), severe illness expected to cause death or disability within 6 months; blood pressure >=180/110 mm Hg; serum creatinine >2.5 mg/dL or dialysis; history of hyponatraemia; use of vitamin supplements greater than the recommended daily allowance; inability to speak English; and lack of a working telephone. Country of publication was the U.S.A.
Interventions	Intervention group: Dehydrated soluble black tea powder was provided to participants in unit-dose containers. Each container included 2.0 g of powder, and 3 containers (representing a single-day supply) were bagged together. The catechin content of the tea was 106 ± 7 mg per serving (i.e. 318 mg/d) of

Mukamal 2007 *(Continued)*

	catechin equivalents. No restrictions were made on addition of milk or sweeteners, reconstitution with hot or cold water, or time of day of consumption. The control group consumed 3 glasses of water daily and dietary restrictions were consumption of non-study tea (green, oolong, or black). Follow-up period was at the end of the intervention period of 6 months.
Outcomes	HDL-cholesterol, LDL-cholesterol, triglycerides, adverse effects.
Notes	Authors contacted for extra information on blood pressure. Authors responded.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Used random permuted blocks of sizes 2 and 4
Allocation concealment (selection bias)	Low risk	Used opaque, sealed, sequentially numbered envelopes in a locked, off-site location
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants knew whether they were in the intervention or control group as they were asked to drink tea or water
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All measurements performed by technicians or investigators blinded to treatment assignment
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis used and attrition and exclusions were reported with reasons
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge
Other bias	Unclear risk	Insufficient information to judge

Nantz 2009

Methods	RCT of parallel group design
Participants	124 healthy adults recruited from University of Florida and Gainsville community (52 males, 72 females), mean age 29. Participants were randomised to 2 arms - Camellia Sinensis capsules (61) and placebo (63). Exclusion criteria: vegetarian diet, chemotherapy or other immune suppressing therapy within the previous year, chronic antibiotics or other infectious disease prophylactic, chronic or current illness, surgery within the previous year, and pregnancy and/or lactation, those who daily consumed greater than one cup (250 mL) of tea, an average of seven or more servings of fruits and vegetables, and herbal supplements and vitamins other than a multivitamin or vitamin D. Country of publication was the U.S.A.
Interventions	Participants were required to consume either 1 Camellia sinensis composition (CSC) capsule or 1 placebo capsule (PBO), twice daily (1 in the morning and 1 in the evening, preferably with meals) for 3 months. CSC capsules contained 100 mg of L-theanine and 200 mg of a decaffeinated catechin green tea extract. PBO capsules contained microcrystalline cellulose, dextrose, dicalcium phosphate, magnesium stearate, silicon dioxide, and FD&C red #40, yellow #6, and blue #1. PBO capsules were identical in

Nantz 2009 *(Continued)*

	appearance to the CSC capsules. Follow-up was at the end of the intervention period of 3 months (90 days).
Outcomes	Blood pressure (systolic and diastolic), adverse effects
Notes	No participant started any new medication during the study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Drawing coloured marbles to allocate to intervention or control group
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	States double-blind and placebo-controlled. Particpants and investigators were blinded to treatment allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	States double-blind but provides no details
Incomplete outcome data (attrition bias) All outcomes	Low risk	Withdrawals and exclusions were clearly reported
Selective reporting (reporting bias)	Unclear risk	Insufficient information to judge
Other bias	Unclear risk	Insufficient information to judge

Shen 2010

Methods	RCT of parallel group design
Participants	Postmenopausal women were recruited through flyers, local TV, radios, newspaper, municipal community centres and clinics. 171 women were randomised into 4 arms - placebo; green tea polyphenols; placebo + tai chi; and green tea polyphenols + tai chi. Inclusion criteria were postmenopausal women (at least 2 years after menopause) with osteopenia; normal function of thyroid, liver and kidney; serum alkaline phosphatase, calcium and inorganic phosphorus within normal ranges; and serum 25-hydroxy vitamin D (25(OH)D) ≥ 20 ng/mL. Exclusion criteria: participants with a disease condition or those on medication known to affect bone metabolism; a history of cancer except for treated superficial basal or squamous cell carcinoma of the skin; uncontrolled intercurrent illness or physical condition that would be a contraindication to exercise; depression; cognitive impairment; or those unwilling to accept randomisation. 47 participants were randomised to receive green tea polyphenols (mean age 56.5, 10.6% with history of diabetes) and 44 randomised to receive placebo (mean age 57.6, 2.3% with history of diabetes). Country of publication was the U.S.A.
Interventions	Green tea polyphenols (GTP) group: GTP 500 mg daily. The main GTP components were 46.5% of epigallocatechin-3-gallate (EGCG), 21.25% of epigallocatechin (ECG), 10% of epicatechin (EC), 7.5% of epicatechin-3-gallate (EGC), 9.5% of gallocatechin gallate (GCG), and 4.5% of catechin. Placebo group:

Shen 2010 *(Continued)*

	medicinal starch 500 mg daily. The daily dose of GTP or placebo material was divided into two capsules (250 mg each). During the 24-week intervention, all participants were provided with 500 mg elemental calcium and 200 IU vitamin D (as cholecalciferol) daily. Follow-up period was at the end of the intervention period of 24 weeks.
Outcomes	Quality of life (8 domains), adverse effects.
Notes	Data only used from two arms: placebo, green tea polyphenol. The reported adverse effects were judged by the safety monitoring team as unlikely to be related to the study protocol.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to judge
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants and investigators responsible for day-to-day operation and data analyses were blinded to the intervention and placebo groups
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Participants and investigators responsible for day-to-day operation and data analyses were blinded to the intervention and placebo groups
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	ITT analysis performed but no reasons reported for loss to follow-up
Selective reporting (reporting bias)	Low risk	All expected outcomes reported
Other bias	Unclear risk	Insufficient information to judge

Smith 2010

Methods	RCT
Participants	Women who volunteered to participate. 27 sedentary women classified as "overweight" were randomised into 4 arms - exercise and active supplement; exercise and placebo; placebo; active supplement. Inclusion criteria were women aged 18-45 years; < 30 min physical activity per week. Exclusion criteria: those with a history of hypertension or metabolic, renal, hepatic, musculoskeletal, autoimmune, or neurological disease; used any medication that might have significantly affected the study outcome; used nutritional supplements, other than a multivitamin, that might have affected metabolism and/or muscle mass within the four weeks prior to the start of the study. 7 participants were randomised to receive the active supplement (Green tea extract) (mean age 27.86) and 5 participants were randomised to the placebo (mean age 28.40). Country of publication was the U.S.A.
Interventions	Active Supplement group: Drink consisted of 10 kcal, B6 and B12, blend of taurine, guarana extract, green tea leaf extract (EGCG), caffeine, glucuronolactone and ginger extract.

Smith 2010 *(Continued)*

	Placebo group: consisted of the same calorie and vitamin content as active supplement. 1 drink a day with time of beverage consumption left to subjects discretion. all beverages were labelled identically and matched for taste and colour.
Outcomes	Total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, blood pressure (systolic and diastolic)
Notes	Data only used from 2 arms: placebo and active supplementation group.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	States double-blind and placebo controlled
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	States double- blind but provides no details
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No ITT analysis used and no loss to follow-up reported
Selective reporting (reporting bias)	Low risk	All expected outcomes reported
Other bias	Unclear risk	Insufficient information to judge

Stendell-Hollis 2010

Methods	RCT
Participants	Women who volunteered to participate. 54 overweight breast cancer survivors were randomised into two arms - green tea or placebo. Inclusion criteria: BMI between 25-40 kg m^{-2}, received chemotherapy for treatment of invasive breast cancer, aged 18-80 years, reported no current tobacco use and have no chronic illnesses. Participants had to be willing to refrain from all weight loss diets and supplements for a study period of six months. Twenty-nine participants were randomised to receive green tea (mean age 56.6) and twenty five participants were randomised to the placebo group (mean age 57.8). Country of publication was the U.S.A.
Interventions	Green tea group: Consumed green tea. Green tea bags comprising of 550-700 mg tea solids, providing an average catechin dose of 58.91 mg and 32.21 mg of EGCG per bag. Participants were to consume 960 mL green tea daily. Individiual tea bags were placed in a provided tea mug with 240 mL of boiling water and allowed to steep for 3 minutes. Green tea was to be consumed four times a day and up to two doses were allowed at any single dosing.

Stendell-Hollis 2010 *(Continued)*

	Placebo group:Citrus-based herbal tea that contained no EGCG. Follow-up period was six months.
Outcomes	Total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Used a table of random numbers
Allocation concealment (selection bias)	Low risk	Allocation done by someone independent of study
Blinding of participants and personnel (performance bias) All outcomes	Low risk	States double-blind and placebo controlled
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	States double-blind but does not provide details
Incomplete outcome data (attrition bias) All outcomes	High risk	No ITT analysis and 36% of participants in the control group and 20% of participants in the intervention group were lost to follow-up
Selective reporting (reporting bias)	Low risk	All expected outcomes reported
Other bias	Unclear risk	Insufficient information to judge

BMI: body mass index
HDL: high-density lipoprotein
ITT: intention-to-treat
LDL: low-density lipoprotein
MRI: magnetic resonance imaging
RCT: randomised controlled trial

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Alexopoulos 2008	Short-term trial (follow-up period was 120 minutes)
Alexopoulos 2009	Short-term trial (follow-up period was 2 weeks)
Arima 2009	Short-term trial (follow-up period was 6 hours)
Auvichayapat 2008	Study focused on weight loss
Basu 2010	Short-term trial (follow-up period was 8 weeks)
Basu 2011	Short-term trial (follow-up period was 8 weeks)

Study	Reason for exclusion
Batista 2009	Short-term trial (follow-up period was 8 weeks)
Belza 2009	Short-term trial (follow-up period was 4 hours)
Bingham 1997	Short-term trial (follow-up period was 4 weeks)
Brown 2011	Short-term trial (follow-up period was 6 weeks)
Davies 2003	Short-term trial (follow-up period was 3 weeks)
de Maat 2000	Short-term trial (follow-up period was 4 weeks)
Di Pierro 2009	Study focused on weight loss
Eichenberger 2010	Short-term trial (follow-up period was 21 days)
Erba 2005	Short-term trial (follow-up period was 42 days)
Fisunoglu 2010	Short-term trial (follow-up period was 6 weeks)
Frank 2009	Short-term trial (follow-up period was 3 weeks)
Freese 1999	Short-term trial (follow-up period was 4 weeks)
Gordillo-Bastidas 2011	Study focused on weight loss
Grassi 2009	Short-term trial (follow-up period was 1 week)
Hakim 2003	No outcomes of interest
Hirata 2004	Short-term trial (follow-up was 2 hours duration)
Hodgson 1999	Short-term trial (follow-up period was 7 days)
Hodgson 2000	No outcomes of interest
Hodgson 2001	No outcomes of interest
Hodgson 2002a	Short-term trial (follow-up period was 4 weeks)
Hodgson 2002b	Short-term trial (follow-up period 7days or 4 weeks)
Hodgson 2002c	Short-term trial (follow-up period 4hrs)
Hodgson 2003	Short-term trial (follow-up period was 4 weeks)
Inami 2007	Short-term trial (follow-up period was 4 weeks)
Ishikawa 1997	Short-term trial (follow-up period was 4 weeks)
Kurita 2010	Short-term trial (follow-up period 8 weeks)
Miller 2012	Short-term trial (follow-up period 90 minutes)
Muroyama 2006	Study focused on weight loss

Study	Reason for exclusion
Nagaya 2004	Short-term trial (follow-up period was 2 hours)
Penugonda 2009	Short-term trial (follow-up period was 8 weeks)
Princen 1998	Short-term trial (follow-up period was 4 weeks)
Quinlan 1997	Short-term trial (follow-up period was 60 minutes)
Quinlan 2000	Short-term trials (follow-up periods were between 60-105 minutes)
Rakic 1996	Short-term trial (follow-up period was 2 weeks)
Ryu 2006	More than 25% of patients had T2D
Schmidschonbein 1991	Short-term trial (follow-up period was 7 hours)
Schultz 2009	Study focused on weight loss
Steptoe 2007	Short-term trial (follow-up period was 6 weeks)
Takase 2008	Study focused on weight loss
Takeshita 2008	Study focused on weight loss
Trautwein 2010	Short-term trial (follow-up period was 11 weeks)
Unno 2005	Short-term trial (follow-up period was 6 hours)
Vlachopoulos 2006	Short-term trial (follow-up period was 3 hours)
Wang 2010	Study focused on weight loss
Wu 2012	Short-term trial (follow-up period was 2 months)
Yen 2010	Study focused on weight loss
Yoshikawa 2012	Short-term trial (follow-up period was 1 week)

T2D: type 2 diabetes

Characteristics of studies awaiting assessment *[ordered by study ID]*

Chen 1991

Methods	Article written in Chinese with no English abstract - awaiting translation.
Participants	
Interventions	
Outcomes	
Notes	

Lu 1997

Methods	Article written in Chinese with no English abstract - awaiting translation.
Participants	
Interventions	
Outcomes	
Notes	

Characteristics of ongoing studies *[ordered by study ID]*

Mitsuhiro Yamada 2009

Trial name or title	A randomised, double-blind, placebo-controlled study of effect of green tea on lifestyle-related disease prevention
Methods	Parallel randomised
Participants	Inclusion criteria: Is over 30 years old and under 75 years old and meets at least one of the followings; 1.BMI:23-35kg/m^2 2.Waist circumference: 85 cm or more in men and 90 cm or more in women Exclusion criteria: 1) Individuals with a medical record of heart failure or cardiac infarction. 2) Individuals judged to have atrial fibrillation, Irregular Heart Beat, hepatic damage, kidney damage, cerebrovascular accident, rheumatism, diabetes mellitus, lipid disorder and/or anaemia. 3) Individuals with a medical record of allergy to food and drug. 4) Pregnant women, or women with intending to become pregnant, and lactating women. 5) Individuals judged by the doctor to be unsuitable. Age minimum: 30 years-old Age maximum: 75 years-old Gender: Men and women Health conditions: metabolic syndrome
Interventions	Ten capsules of green tea powder, three times a day (6 g/day), for 12 weeks. Ten placebo capsules, three times a day (6 g/day), for 12 weeks.
Outcomes	Primary 1) body weight 2) HbA1c 3) LDL-cholesterol Secondary 1) Blood pressure, fat percentage, waist, BMI 2) FBS, insulin 3) Serum total cholesterol, HDL-cholesterol, triglycerides 4) Serum amyloid protein A, high sensitive C_reactive protein 5) Adiponectin, TNF-alfa, urine 8-OHdG

Mitsuhiro Yamada 2009 *(Continued)*

Starting date	Date of first enrolment: 2009/02/01
Contact information	Mitsuhiro Yamada Address: 9-28, Goshohara, Kakegawa, Shizuoka, Japan Email: mdysame@yahoo.co.jp
Notes	

BMI: body mass index
FBS: fasting blood sugar
HDL: high-density lipoprotein
LDL: low-density lipoprotein
TNF: tumour necrosis factor

DATA AND ANALYSES

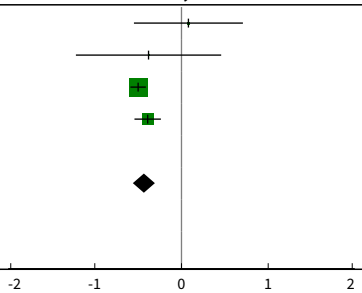
Comparison 1. Black Tea

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 LDL-Cholesterol	4	147	Mean Difference (IV, Random, 95% CI)	-0.43 [-0.56, -0.31]
2 HDL-Cholesterol	4	146	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.06, 0.04]
3 Triglycerides	4		Mean Difference (IV, Random, 95% CI)	Totals not selected
4 Total Cholesterol	3		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5 Systolic blood pressure	2	123	Mean Difference (IV, Fixed, 95% CI)	-1.85 [-3.21, -0.48]
6 Diastolic blood pressure	2	123	Mean Difference (IV, Fixed, 95% CI)	-1.27 [-3.06, 0.53]

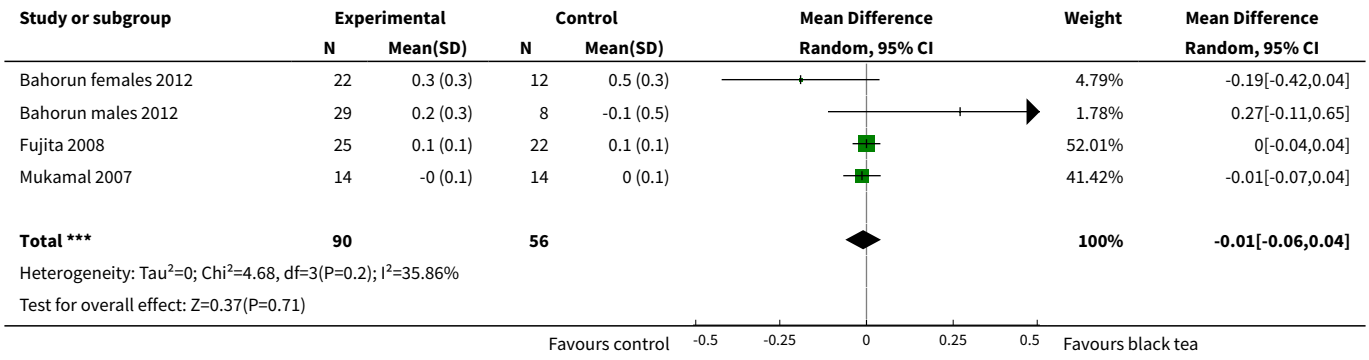
Analysis 1.1. Comparison 1 Black Tea, Outcome 1 LDL-Cholesterol.

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Bahorun females 2012	22	0.4 (1.1)	11	0.3 (0.7)		3.9%	0.08[-0.55,0.71]
Bahorun males 2012	31	-0.1 (1.1)	8	0.3 (1.1)		2.24%	-0.38[-1.22,0.46]
Fujita 2008	25	-0.5 (0.2)	22	-0 (0.2)		56.84%	-0.5[-0.59,-0.41]
Mukamal 2007	14	-0.3 (0.3)	14	0.1 (0.1)		37.02%	-0.39[-0.54,-0.24]
Total ***	**92**		**55**			**100%**	**-0.43[-0.56,-0.31]**

Heterogeneity: Tau^2=0.01; Chi^2=4.45, df=3(P=0.22); I^2=32.62%
Test for overall effect: Z=6.68(P<0.0001)



Analysis 1.2. Comparison 1 Black Tea, Outcome 2 HDL-Cholesterol.

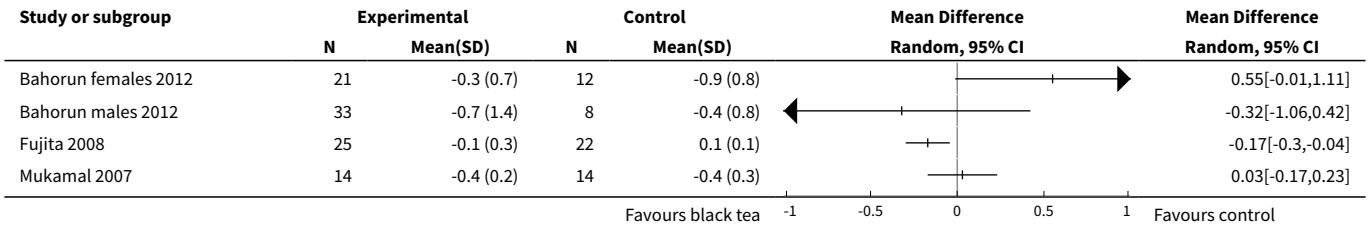


Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Bahorun females 2012	22	0.3 (0.3)	12	0.5 (0.3)		4.79%	-0.19[-0.42,0.04]
Bahorun males 2012	29	0.2 (0.3)	8	-0.1 (0.5)		1.78%	0.27[-0.11,0.65]
Fujita 2008	25	0.1 (0.1)	22	0.1 (0.1)		52.01%	0[-0.04,0.04]
Mukamal 2007	14	-0 (0.1)	14	0 (0.1)		41.42%	-0.01[-0.07,0.04]
Total ***	**90**		**56**			**100%**	**-0.01[-0.06,0.04]**

Heterogeneity: Tau²=0; Chi²=4.68, df=3(P=0.2); I²=35.86%

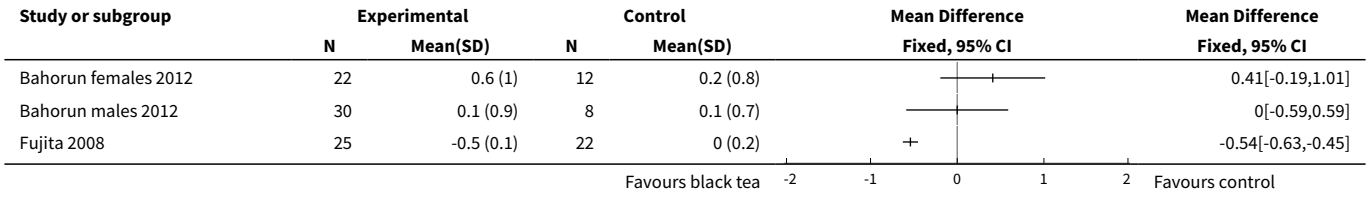
Test for overall effect: Z=0.37(P=0.71)

Analysis 1.3. Comparison 1 Black Tea, Outcome 3 Triglycerides.



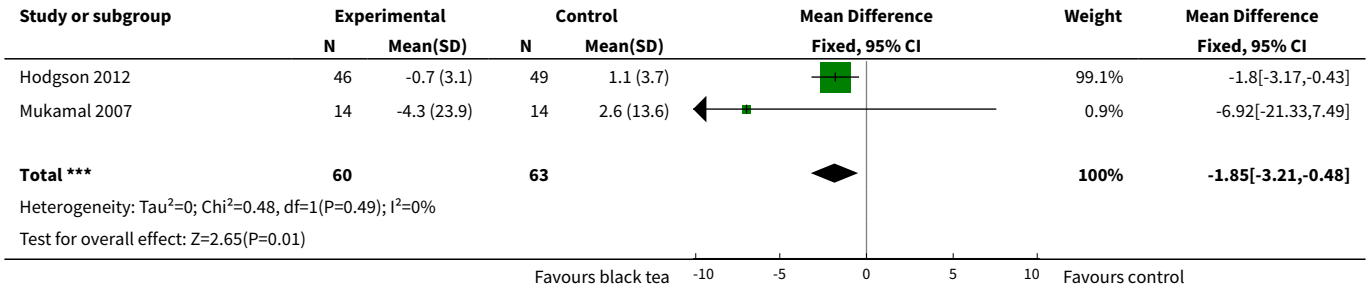
Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Bahorun females 2012	21	-0.3 (0.7)	12	-0.9 (0.8)		0.55[-0.01,1.11]
Bahorun males 2012	33	-0.7 (1.4)	8	-0.4 (0.8)		-0.32[-1.06,0.42]
Fujita 2008	25	-0.1 (0.3)	22	0.1 (0.1)		-0.17[-0.3,-0.04]
Mukamal 2007	14	-0.4 (0.2)	14	-0.4 (0.3)		0.03[-0.17,0.23]

Analysis 1.4. Comparison 1 Black Tea, Outcome 4 Total Cholesterol.



Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Bahorun females 2012	22	0.6 (1)	12	0.2 (0.8)		0.41[-0.19,1.01]
Bahorun males 2012	30	0.1 (0.9)	8	0.1 (0.7)		0[-0.59,0.59]
Fujita 2008	25	-0.5 (0.1)	22	0 (0.2)		-0.54[-0.63,-0.45]

Analysis 1.5. Comparison 1 Black Tea, Outcome 5 Systolic blood pressure.

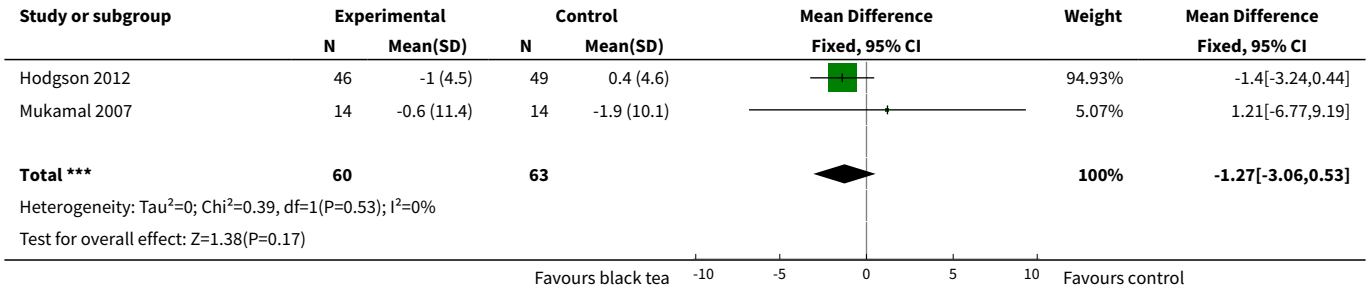


Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Hodgson 2012	46	-0.7 (3.1)	49	1.1 (3.7)		99.1%	-1.8[-3.17,-0.43]
Mukamal 2007	14	-4.3 (23.9)	14	2.6 (13.6)		0.9%	-6.92[-21.33,7.49]
Total ***	**60**		**63**			**100%**	**-1.85[-3.21,-0.48]**

Heterogeneity: Tau²=0; Chi²=0.48, df=1(P=0.49); I²=0%

Test for overall effect: Z=2.65(P=0.01)

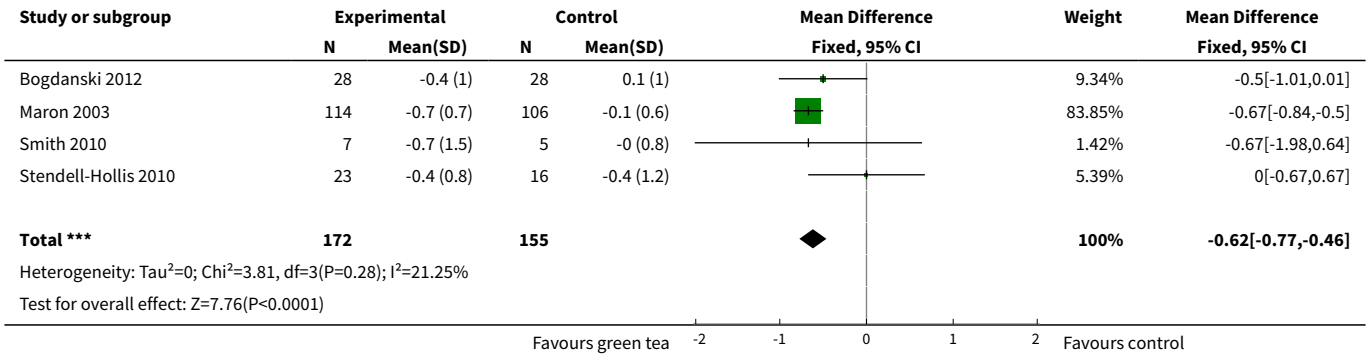
Analysis 1.6. Comparison 1 Black Tea, Outcome 6 Diastolic blood pressure.



Comparison 2. Green Tea

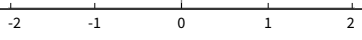
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total Cholesterol	4	327	Mean Difference (IV, Fixed, 95% CI)	-0.62 [-0.77, -0.46]
2 LDL Cholesterol	4	327	Mean Difference (IV, Fixed, 95% CI)	-0.64 [-0.77, -0.52]
3 Triglycerides	4	327	Mean Difference (IV, Fixed, 95% CI)	-0.08 [-0.24, 0.07]
4 HDL-Cholesterol	4	327	Mean Difference (IV, Random, 95% CI)	0.01 [-0.08, 0.11]
5 Systolic Blood Pressure	2	167	Mean Difference (IV, Fixed, 95% CI)	-3.18 [-5.25, -1.11]
6 Diastolic Blood Pressure	2	167	Mean Difference (IV, Fixed, 95% CI)	-3.42 [-4.54, -2.30]

Analysis 2.1. Comparison 2 Green Tea, Outcome 1 Total Cholesterol.



Analysis 2.2. Comparison 2 Green Tea, Outcome 2 LDL Cholesterol.

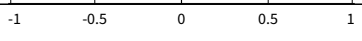
Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Bogdanski 2012	28	-0.4 (1)	28	0 (1.1)		5.55%	-0.4[-0.94,0.14]
Maron 2003	114	-0.7 (0.5)	106	0 (0.5)		90.06%	-0.68[-0.81,-0.55]
Smith 2010	7	-0.7 (1.4)	5	-0.1 (0.8)		1.05%	-0.53[-1.76,0.7]
Stendell-Hollis 2010	23	-0.5 (0.9)	16	-0.4 (1.2)		3.34%	-0.1[-0.79,0.59]
Total ***	**172**		**155**			**100%**	**-0.64[-0.77,-0.52]**
Heterogeneity: Tau^2=0; Chi^2=3.46, df=3(P=0.33); I^2=13.4%							
Test for overall effect: Z=9.95(P<0.0001)							



Favours green tea — Favours control

Analysis 2.3. Comparison 2 Green Tea, Outcome 3 Triglycerides.

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Bogdanski 2012	28	-0.3 (0.6)	28	0 (0.6)		27.34%	-0.3[-0.59,-0.01]
Maron 2003	114	-0 (1)	106	-0 (0.8)		43.89%	0[-0.23,0.23]
Smith 2010	7	0 (0.4)	5	0 (0.4)		12.19%	-0.01[-0.45,0.43]
Stendell-Hollis 2010	23	-0.2 (0.7)	16	-0.2 (0.5)		16.58%	0[-0.38,0.38]
Total ***	**172**		**155**			**100%**	**-0.08[-0.24,0.07]**
Heterogeneity: Tau^2=0; Chi^2=2.89, df=3(P=0.41); I^2=0%							
Test for overall effect: Z=1.06(P=0.29)							



Favours green tea — Favours control

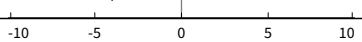
Analysis 2.4. Comparison 2 Green Tea, Outcome 4 HDL-Cholesterol.

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Bogdanski 2012	28	0.2 (0.3)	28	0.1 (0.2)		31.87%	0.1[-0.02,0.22]
Maron 2003	114	-0 (0.3)	106	-0 (0.3)		43.28%	0.03[-0.05,0.11]
Smith 2010	7	-0.1 (0.2)	5	0.1 (0.5)		4%	-0.23[-0.68,0.22]
Stendell-Hollis 2010	23	0.1 (0.2)	16	0.2 (0.3)		20.84%	-0.1[-0.27,0.07]
Total ***	**172**		**155**			**100%**	**0.01[-0.08,0.11]**
Heterogeneity: Tau^2=0; Chi^2=4.91, df=3(P=0.18); I^2=38.92%							
Test for overall effect: Z=0.31(P=0.75)							

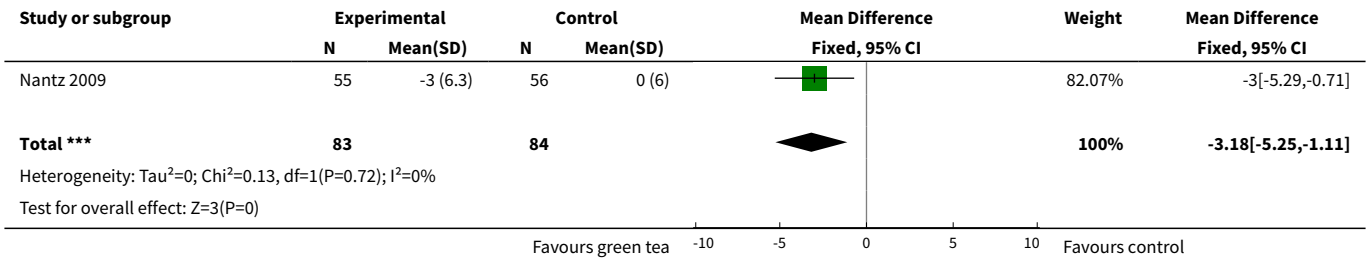
Favours control — Favours green tea

Analysis 2.5. Comparison 2 Green Tea, Outcome 5 Systolic Blood Pressure.

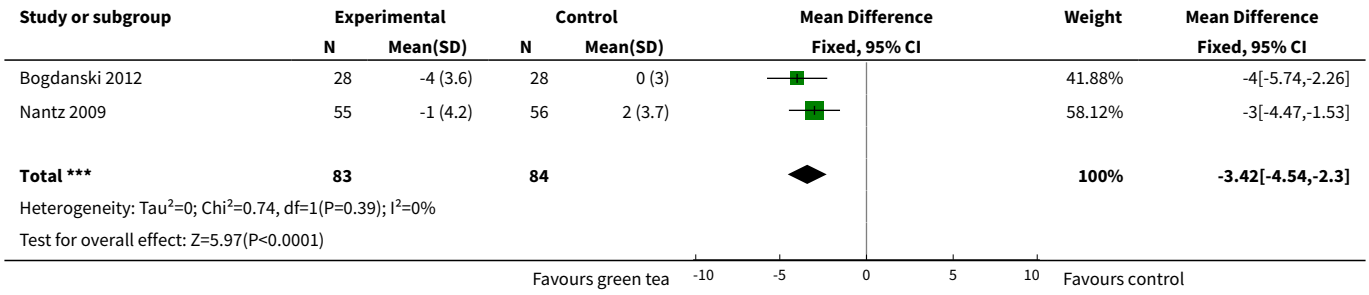
Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Bogdanski 2012	28	-4 (9.2)	28	0 (9.5)		17.93%	-4[-8.9,0.9]



Favours green tea — Favours control



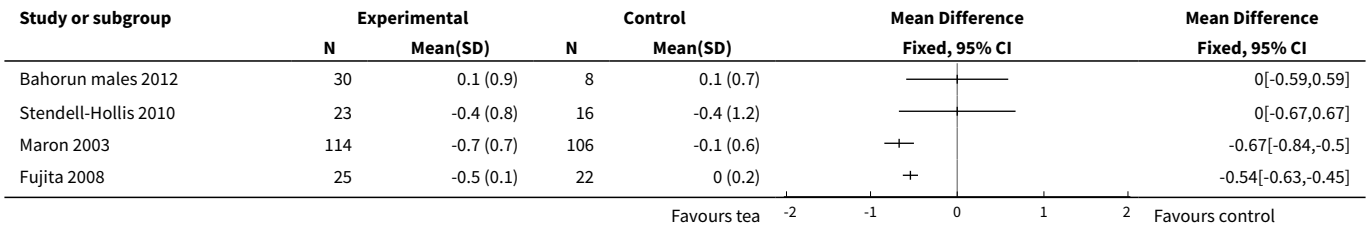
Analysis 2.6. Comparison 2 Green Tea, Outcome 6 Diastolic Blood Pressure.



Comparison 3. All Tea

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total Cholesterol	7		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2 LDL-Cholesterol	8	474	Mean Difference (IV, Random, 95% CI)	-0.48 [-0.61, -0.35]
3 HDL-Cholesterol	8	473	Mean Difference (IV, Random, 95% CI)	0.00 [-0.04, 0.04]
4 Triglycerides	8	476	Mean Difference (IV, Random, 95% CI)	-0.06 [-0.19, 0.06]
5 Systolic Blood Pressure	4	290	Mean Difference (IV, Fixed, 95% CI)	-2.25 [-3.39, -1.11]
6 Diastolic Blood Pressure	4	290	Mean Difference (IV, Fixed, 95% CI)	-2.81 [-3.77, -1.86]

Analysis 3.1. Comparison 3 All Tea, Outcome 1 Total Cholesterol.



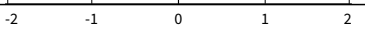
Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
Bogdanski 2012	28	-0.4 (1)	28	0.1 (1)		-0.5[-1.01,0.01]
Bahorun females 2012	22	0.6 (1)	12	0.2 (0.8)		0.41[-0.19,1.01]
Smith 2010	7	-0.7 (1.5)	5	-0 (0.8)		-0.67[-1.98,0.64]

Analysis 3.2. Comparison 3 All Tea, Outcome 2 LDL-Cholesterol.

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Bahorun females 2012	22	0.4 (1.1)	11	0.3 (0.7)		3.89%	0.08[-0.55,0.71]
Bahorun males 2012	31	-0.1 (1.1)	8	0.3 (1.1)		2.29%	-0.38[-1.22,0.46]
Bogdanski 2012	28	-0.4 (1)	28	0 (1.1)		5.11%	-0.4[-0.94,0.14]
Fujita 2008	25	-0.5 (0.2)	22	-0 (0.2)		32.2%	-0.5[-0.59,-0.41]
Maron 2003	114	-0.7 (0.5)	106	0 (0.5)		27.14%	-0.68[-0.81,-0.55]
Mukamal 2007	14	-0.3 (0.3)	14	0.1 (0.1)		25.02%	-0.39[-0.54,-0.24]
Smith 2010	7	-0.7 (1.4)	5	-0.1 (0.8)		1.09%	-0.53[-1.76,0.7]
Stendell-Hollis 2010	23	-0.5 (0.9)	16	-0.4 (1.2)		3.26%	-0.1[-0.79,0.59]
Total ***	**264**		**210**			**100%**	**-0.48[-0.61,-0.35]**

Heterogeneity: Tau^2=0.01; Chi^2=13.64, df=7(P=0.06); I^2=48.66%

Test for overall effect: Z=7.16(P<0.0001)



Analysis 3.3. Comparison 3 All Tea, Outcome 3 HDL-Cholesterol.

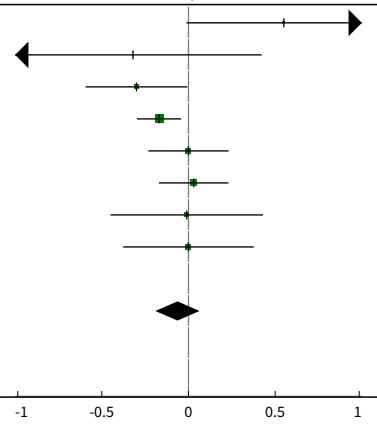
Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Bahorun females 2012	22	0.3 (0.3)	12	0.5 (0.3)		3.44%	-0.19[-0.42,0.04]
Bahorun males 2012	29	0.2 (0.3)	8	-0.1 (0.5)		1.29%	0.27[-0.11,0.65]
Bogdanski 2012	28	0.2 (0.3)	28	0.1 (0.2)		10.57%	0.1[-0.02,0.22]
Fujita 2008	25	0.1 (0.1)	22	0.1 (0.1)		33.32%	0[-0.04,0.04]
Maron 2003	114	-0 (0.3)	106	-0 (0.3)		17.28%	0.03[-0.05,0.11]
Mukamal 2007	14	-0 (0.1)	14	0 (0.1)		27.21%	-0.01[-0.07,0.04]
Smith 2010	7	-0.1 (0.2)	5	0.1 (0.5)		0.94%	-0.23[-0.68,0.22]
Stendell-Hollis 2010	23	0.1 (0.2)	16	0.2 (0.3)		5.94%	-0.1[-0.27,0.07]
Total ***	**262**		**211**			**100%**	**0[-0.04,0.04]**

Heterogeneity: Tau^2=0; Chi^2=10.42, df=7(P=0.17); I^2=32.85%

Test for overall effect: Z=0.05(P=0.96)

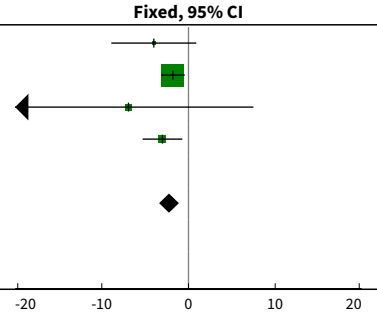
Analysis 3.4. Comparison 3 All Tea, Outcome 4 Triglycerides.

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Bahorun females 2012	21	-0.3 (0.7)	12	-0.9 (0.8)		4.56%	0.55[-0.01,1.11]
Bahorun males 2012	33	-0.7 (1.4)	8	-0.4 (0.8)		2.75%	-0.32[-1.06,0.42]
Bogdanski 2012	28	-0.3 (0.6)	28	0 (0.6)		12.67%	-0.3[-0.59,-0.01]
Fujita 2008	25	-0.1 (0.3)	22	0.1 (0.1)		27.67%	-0.17[-0.3,-0.04]
Maron 2003	114	-0 (1)	106	-0 (0.8)		16.93%	0[-0.23,0.23]
Mukamal 2007	14	-0.4 (0.2)	14	-0.4 (0.3)		19.66%	0.03[-0.17,0.23]
Smith 2010	7	0 (0.4)	5	0 (0.4)		6.92%	-0.01[-0.45,0.43]
Stendell-Hollis 2010	23	-0.2 (0.7)	16	-0.2 (0.5)		8.84%	0[-0.38,0.38]
Total ***	**265**		**211**			**100%**	**-0.06[-0.19,0.06]**
Heterogeneity: Tau^2=0.01; Chi^2=11.15, df=7(P=0.13); I^2=37.2%							
Test for overall effect: Z=0.98(P=0.33)							



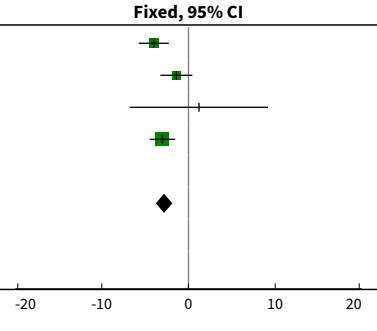
Analysis 3.5. Comparison 3 All Tea, Outcome 5 Systolic Blood Pressure.

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Bogdanski 2012	28	-4 (9.2)	28	0 (9.5)		5.42%	-4[-8.9,0.9]
Hodgson 2012	46	-0.7 (3.1)	49	1.1 (3.7)		69.13%	-1.8[-3.17,-0.43]
Mukamal 2007	14	-4.3 (23.9)	14	2.6 (13.6)		0.63%	-6.92[-21.33,7.49]
Nantz 2009	55	-3 (6.3)	56	0 (6)		24.82%	-3[-5.29,-0.71]
Total ***	**143**		**147**			**100%**	**-2.25[-3.39,-1.11]**
Heterogeneity: Tau^2=0; Chi^2=1.72, df=3(P=0.63); I^2=0%							
Test for overall effect: Z=3.86(P=0)							



Analysis 3.6. Comparison 3 All Tea, Outcome 6 Diastolic Blood Pressure.

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Bogdanski 2012	28	-4 (3.6)	28	0 (3)		30.11%	-4[-5.74,-2.26]
Hodgson 2012	46	-1 (4.5)	49	0.4 (4.6)		26.67%	-1.4[-3.24,0.44]
Mukamal 2007	14	-0.6 (11.4)	14	-1.9 (10.1)		1.42%	1.21[-6.77,9.19]
Nantz 2009	55	-1 (4.2)	56	2 (3.7)		41.79%	-3[-4.47,-1.53]
Total ***	**143**		**147**			**100%**	**-2.81[-3.77,-1.86]**
Heterogeneity: Tau^2=0; Chi^2=5.09, df=3(P=0.17); I^2=41.05%							
Test for overall effect: Z=5.79(P<0.0001)							



ADDITIONAL TABLES

Table 1. Short term trials of tea intake (<3 months duration)

Study	Green/Black or extracts?	Dose	Duration
Alexopoulos 2009	Black and Green tea	6 g/d	2 wks
Basu 2011	Green tea and Green tea extract	4 cups/d or 2 capsules and 4 cups of water /d	8 wks
Basu 2010	Green tea and Green tea extract	4 cups/d or 2 capsules and 4 cups of water /d	8 wks
Batista 2009	Green tea extract	250 mg/d	8 wks
Belza 2009	Green tea extract	500 mg	4 hrs
Bingham 1997	Black tea	6 mugs/d	4 wks
Brown 2011	Green tea extract	530 mg twice a day	6 wks
Davies 2003	Black tea	5 servings a day	3 wks
de Maat 2000	Black tea, Green tea and Green tea extract	6 cups (150 mL)/day or 6 x 4 capsules/day with 6 x 150 mL of control beverage	4 wks
Eichenberger 2010	Green tea extract	In a beverage consumed once a day	21 days
Fisunoglu 2010	Black tea	5 servings (200 mL)/d	6 wks
Frank 2009	Green tea extract	6 capsules/d	3 wks
Freese 1999	Green tea extract	3 g a day	4 wks
Grassi 2009	Black tea	0mg, 100 mg, 200 mg, 400 mg or 800 mg twice a day	1 wk
Hirata 2004	Black tea	450 mL	2hrs
Hodgson 2003	Black tea	1250 mL/d	4 wks
Hodgson 1999	Black or Green tea	5 cups/d	7 d
Hodgson 2002a	Black tea	5 cups/d	4 wks
Inami 2007	Green tea extract	500 mg	4 wks
Ishikawa 1997	Black tea	5 cups/d (750 mL)	4 wks
Kurita 2010	Black tea	> 200 mL twice a day	8 wks
Nagaya 2004	Green tea	400ml	2 hrs
Penugonda 2009	Green tea or Green tea extract	4 cups a day or 2 capsules and 4 cups of water a day	8 wks
Princen 1998	Black or Green tea	6 cups/d of Black or Green tea or 3,6g tablet of Green tea polyphenols/day	4 wks

Table 1. Short term trials of tea intake (<3 months duration) *(Continued)*

Quinlan 1997	Black tea	400 mL	60 mins
Quinlan 2000	Black tea	300 mL	105 mins
Rakic 1996	Black tea	5 cups per day	2 weeks
Schmidschonbein 1991	Black tea	1 litre	7 hours
Trautwein 2010	Black tea extract	one capsule/d	11 wks
Vlachopoulos 2006	Black or Green tea	6 gm	3 hrs
Hodgson 2002b	Black and Green tea	1000 mL/d or 250 mL/d	7 d or 4 wks
Hodgson 2002c	Black tea	one cup	4 hrs
Miller 2012	Green tea extract	1.06 g	90 mins
Erba 2005	Green tea	2 cups	42 days
Wu 2012	Green tea extract	400 mg or 800 mg per day	2 mths
Alexopoulos 2008	Green tea	6 g	120 mins
Arima 2009	Black tea	1 cup	6 hours
Unno 2005	Tea	10, 224 or 674 mg of tea catechins	6 hours
Yoshikawa 2012	Tea	1069 mg/day of total catechins	1 wk
Steptoe 2007	Black tea	4 sachets a day	6 wks

d:day

APPENDICES

Appendix 1. Search strategies October 2012

CENTRAL, DARE, HTA, HEE on The Cochrane Library

#1 MeSH descriptor: [Cardiovascular Diseases] explode all trees
#2 cardio*
#3 cardia*
#4 heart*
#5 coronary*
#6 angina*
#7 ventric*
#8 myocard*
#9 pericard*
#10 isch?em*
#11 emboli*
#12 arrhythmi*
#13 thrombo*
#14 atrial next fibrillat*
#15 tachycardi*
#16 endocardi*

#17 sick near sinus
#18 MeSH descriptor: [Stroke] explode all trees
#19 stroke or stokes
#20 cerebrovasc*
#21 cerebral next vascular
#22 apoplexy
#23 brain near/2 accident*
#24 brain* near/2 infarct*
#25 cerebral near/2 infarct*
#26 lacunar near/2 infarct*
#27 MeSH descriptor: [Hypertension] explode all trees
#28 hypertensi*
#29 peripheral next arter* next disease*
#30 high near/2 blood next pressure
#31 increased near/2 blood next pressure
#32 elevated near/2 blood next pressure
#33 MeSH descriptor: [Hyperlipidemias] explode all trees
#34 hyperlipid*
#35 hyperlip?emia*
#36 hypercholesterol*
#37 hypercholester?emia*
#38 hyperlipoprotein?emia*
#39 hypertriglycerid?emia*
#40 MeSH descriptor: [Arteriosclerosis] explode all trees
#41 MeSH descriptor: [Cholesterol] explode all trees
#42 cholesterol
#43 "coronary risk factor*"
#44 MeSH descriptor: [Blood Pressure] this term only
#45 "blood pressure"
#46 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45
#47 MeSH descriptor: [Tea] this term only
#48 tea or teas
#49 (green and black) near/3 (tea or teas)
#50 (tea or teas) near/3 (extract*)
#51 MeSH descriptor: [Catechin] this term only
#52 (catechuic or catechinic or catechin)
#53 cyanidanol
#54 zyma
#55 epicatechin
#56 kb 53
#57 flavanpentol
#58 z 7300
#59 catergen*
#60 #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59
#61 #46 and #60

MEDLINE OVID

1. exp Cardiovascular Diseases/
2. cardio*.tw.
3. cardia*.tw.
4. heart*.tw.
5. coronary*.tw.
6. angina*.tw.
7. ventric*.tw.
8. myocard*.tw.
9. pericard*.tw.
10. isch?em*.tw.
11. emboli*.tw.
12. arrhythmi*.tw.

13. thrombo*.tw.
14. atrial fibrillat*.tw.
15. tachycardi*.tw.
16. endocardi*.tw.
17. (sick adj sinus).tw.
18. exp Stroke/
19. (stroke or stokes).tw.
20. cerebrovasc*.tw.
21. cerebral vascular.tw.
22. apoplexy.tw.
23. (brain adj2 accident*).tw.
24. ((brain* or cerebral or lacunar) adj2 infarct*).tw.
25. exp Hypertension/
26. hypertensi*.tw.
27. peripheral arter* disease*.tw.
28. ((high or increased or elevated) adj2 blood pressure).tw.
29. exp Hyperlipidemias/
30. hyperlipid*.tw.
31. hyperlip?emia*.tw.
32. hypercholesterol*.tw.
33. hypercholester?emia*.tw.
34. hyperlipoprotein?emia*.tw.
35. hypertriglycerid?emia*.tw.
36. exp Arteriosclerosis/
37. exp Cholesterol/
38. cholesterol.tw.
39. "coronary risk factor*".tw.
40. Blood Pressure/
41. blood pressure.tw.
42. or/1-41
43. Tea/
44. (tea or teas).tw.
45. ((green or black) adj3 (tea or teas)).tw.
46. ((tea or teas) adj3 extract$).tw.
47. Catechin/
48. (catechuic or catechinic or catechin).tw.
49. cyanidanol.tw.
50. zyma.tw.
51. epicatechin.tw.
52. kb 53.tw.
53. flavanpentol.tw.
54. z 7300.tw.
55. catergen$.tw.
56. or/43-55
57. 42 and 56
58. randomized controlled trial.pt.
59. controlled clinical trial.pt.
60. randomized.ab.
61. placebo.ab.
62. drug therapy.fs.
63. randomly.ab.
64. trial.ab.
65. groups.ab.
66. 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65
67. exp animals/ not humans.sh.
68. 66 not 67
69. 57 and 68

EMBASE OVID

1. exp cardiovascular disease/
2. cardio*.tw.

3. cardia*.tw.
4. heart*.tw.
5. coronary*.tw.
6. angina*.tw.
7. ventric*.tw.
8. myocard*.tw.
9. pericard*.tw.
10. isch?em*.tw.
11. emboli*.tw.
12. arrhythmi*.tw.
13. thrombo*.tw.
14. atrial fibrillat*.tw.
15. tachycardi*.tw.
16. endocardi*.tw.
17. (sick adj sinus).tw.
18. exp cerebrovascular disease/
19. (stroke or stokes).tw.
20. cerebrovasc*.tw.
21. cerebral vascular.tw.
22. apoplexy.tw.
23. (brain adj2 accident*).tw.
24. ((brain* or cerebral or lacunar) adj2 infarct*).tw.
25. exp hypertension/
26. hypertensi*.tw.
27. peripheral arter* disease*.tw.
28. ((high or increased or elevated) adj2 blood pressure).tw.
29. exp hyperlipidemia/
30. hyperlipid*.tw.
31. hyperlip?emia*.tw.
32. hypercholesterol*.tw.
33. hypercholester?emia*.tw.
34. hyperlipoprotein?emia*.tw.
35. hypertriglycerid?emia*.tw.
36. exp Arteriosclerosis/
37. exp Cholesterol/
38. cholesterol.tw.
39. "coronary risk factor*".tw.
40. Blood Pressure/
41. blood pressure.tw.
42. or/1-41
43. tea/
44. green tea extract/
45. black tea extract/
46. (tea or teas).tw.
47. ((green or black) adj3 (tea or teas)).tw.
48. ((tea or teas) adj3 extract$).tw.
49. catechin/
50. (catechuic or catechin).tw.
51. catechinic.tw.
52. cyanidanol.tw.
53. zyma.tw.
54. epicatechin.tw.
55. kb 53.tw.
56. flavanpentol.tw.
57. z 7300.tw.
58. catergen$.tw.
59. or/43-58
60. 42 and 59
61. random$.tw.
62. factorial$.tw.
63. crossover$.tw.
64. cross over$.tw.

65. cross-over$.tw.
66. placebo$.tw.
67. (doubl$ adj blind$).tw.
68. (singl$ adj blind$).tw.
69. assign$.tw.
70. allocat$.tw.
71. volunteer$.tw.
72. crossover procedure/
73. double blind procedure/
74. randomized controlled trial/
75. single blind procedure/
76. 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75
77. (animal/ or nonhuman/) not human/
78. 76 not 77
79. 60 and 78

Web of Science

#36 #35 AND #34 AND #33
#35 #32 OR #31 OR #30 OR #29 OR #28 OR #27 OR #26
#34 #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1
#33 TS=(random* or blind* or allocat* or assign* or trial* or placebo* or crossover* or cross-over*)
#32 TS=(catergen* or (z 7300) or flavanpentol or (kb 53) or epicatechin)
#31 TS=(zyma)
#30 TS=(cyanidanol)
#29 TS=((catechuic or catechinic or catechin))
#28 TS=(((tea or teas) near/3 extract*))
#27 TS=(((green or black) near/3 (tea or teas)))
#26 TS=(tea or teas)
#25 TS=(arteriosclerosis or cholesterol or "coronary risk factor*" or "blood pressure")
#24 TS=(hypercholester?emia* or hyperlipoprotein?emia* or hypertriglycerid?emia*)
#23 TS=(hyperlipid* or hyperlip?emia* or hypercholesterol*)
#22 TS=(((brain* or cerebral or lacunar) near/2 infarct*))
#21 TS=(brain near/2 accident*)
#20 TS=(apoplexy)
#19 TS=("cerebral vascular")
#18 TS=(cerebrovasc*)
#17 TS=(stroke or strokes)
#16 TS=("sick sinus")
#15 TS=(endocardi*)
#14 TS=(tachycardi*)
#13 TS=((atrial fibrillat*))
#12 TS=(thrombo*)
#11 TS=(arrhythmi*)
#10 TS=(emboli*)
#9 TS=(isch?em*)
#8 TS=(pericard*)
#7 TS=(myocard*)
#6 TS=(ventric*)
#5 TS=(angina*)
#4 TS=(coronary*)
#3 TS=(heart*)
#2 TS=(cardia*)
#1 TS=(cardio*)

Appendix 2. Search strategies for trial registers

metaRegister of controlled trials (mRCT), Clinical trials.gov, the WHO International Clinical Trials Registry platform (ICTRP)

1. Green AND/OR Black AND Tea

CONTRIBUTIONS OF AUTHORS

All authors contributed to the protocol development. The Trials Search Co-ordinators of the CHG ran the searches, Review authors LH and NF screened titles and abstracts and assessed studies for formal inclusion and exclusion. LH and NF or JH abstracted data and assessed methodological rigour. NF analysed the data which were checked by KR. LH and NF wrote the first draft of the review and all authors contributed to later drafts.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Warwick Medical School, University of Warwick, UK.
- Norwich Medical School, University of East Anglia, UK.

External sources

- NIHR Cochrane Programme Grant, UK.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

It was our intention to perform stratified analysis to examine the effects of caffeine content and “dose” and duration of the intervention but the review included an insufficient number of trials to do this. Similarly, the lack of included studies meant that we were unable to examine the effects of caffeine intake. We also intended to perform funnel plots to assess publication bias. These will be addressed in future updates of this review when more evidence is available.

INDEX TERMS

Medical Subject Headings (MeSH)

*Beverages; *Camellia sinensis; Blood Pressure [physiology]; Cardiovascular Diseases [*prevention & control]; Cholesterol [blood]; Phytotherapy [*methods]; Primary Prevention [*methods]; Randomized Controlled Trials as Topic; Tea

MeSH check words

Humans